GENERAL BIOCHEMISTRY

PETERSON and STRONG

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PREFACE

This book considers the chemical activities not only of animals but also those of plants and microorganisms. It aims to be a complete, though brief, treatise on the whole field of biochemistry, stressing the most important features of the subject.

The first part deals with the materials of the cell, and the second with the functions of the cell. Emphasis, however, has been placed on the dynamic aspects of biochemistry as well as on its material features. This purpose inevitably leads to a consideration of complex phenomena. To make such phenomena understandable is no easy task, but the attempt has been made.

The subject matter is by no means beyond the comprehension of the reader with only a general chemistry background, though best appreciated and understood by the reader with a knowledge of organic chemistry. In view of the increased coverage (chapters on Nucleic Acids, Hormones, and Biological Energetics) and the particular emphasis which has been placed on metabolic reactions (chapters on Plant Metabolism, Animal Metabolism, and Metabolism of Microorganisms), the present work is well suited to more advanced readers. By careful selection of chapters, the book should also prove useful to those interested in agriculture and home economics.

The authors are indebted to their colleagues, Professors Casida, Johnson, Lardy, Meyer, Plaut, Potter, Stahmann, and Williams for reading one or more chapters of the manuscript and making many valuable suggestions and criticisms of the book. They are doubly indebted to Professor Burris for his chapter on Plant Metabolism, and to Professor Plaut for the two chapters on Digestion and Enzymes. The authors are grateful to Dr. Mary Shine Peterson for the preparation of Tables 3–1, 4–2, 5–1, A–1, A–2, and A–3, and for critical reading of many of the chapters in the book.

In making these acknowledgments, the authors in no sense imply that errors of omission and commission are to be charged to those named. We apply to ourselves alone Byron's apostrophe to the ocean, "Upon the watery plain, the wrecks are all thy deed."

W. H. Peterson

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Chapter 1

INTRODUCTION

The living world

Biochemistry, as the name implies, means the chemistry of living things. Obviously such a meaning includes the chemistry of plants and microorganisms, as well as animals. The first two groups are indispensable to a living world, but the third is not. Although a living world composed only of plants and microorganisms would be unfamiliar to us, it would be adequate to maintain a balance between the synthetic processes of the plant and the degradative processes of microorganisms. Put in other terms, the carbon and nitrogen cycles in nature could be kept in balance without the help of animals. The latter are superimposed upon the plants and microorganisms; and man, because of his dominant position in the living world, places himself at its center.

The brief phrase, "chemistry of living things," covers a vast field of subject matter. It includes, in the first place, the chemical make-up of all the individual substances of which living tissues are composed. These substances are extraordinarily numerous. A single cell of the simplest type contains scores, probably hundreds, of different chemical substances —no one knows how many in any particular organism. Furthermore, many of these substances, or *compounds* as the chemist prefers to call them, are extremely complex. Whole classes of biological compounds are so involved that, even today, the exact structural formula of no single member is known; prime examples are the proteins and nucleic acids. Quantitatively, the most important single constituent is *water*. Everything else is classified as *dry matter* or *solids*, which consist mostly of organic compounds (substances containing carbon), although many inorganic substances are present in small amounts.

Secondly, the "chemistry of living things" includes whatever chemical changes the above substances undergo as the organism grows, reproduces, absorbs and uses food, excretes waste products, and in general carries out the activities incidental to being and remaining alive. The sum total of all these chemical processes and the chemical compounds involved in them *is* the living organism. The individual at any moment is a dynamic balance between opposing processes of building up and breaking down, of taking in and throwing off, just as a lake is the resultant of the inflow and outflow of its waters.

Objectives and methods of biochemistry

The ultimate objectives of the science of biochemistry are a complete knowledge of the structure and properties of all chemical compounds present in living things and a complete understanding of the chemical reactions they undergo both in health and disease. Usually, knowledge of materials must first be obtained before much can be learned about their function. At the present time the chief types of organic substance in most biological materials are fairly well known. These major components are the carbohydrates, fats and proteins. However, it has become increasingly clear during the last few decades that many compounds, *e.g.*, vitamins and hormones, normally present in living cells in only very small amounts often play important physiological roles. An impressive number of these compounds is now known, but many more certainly remain to be studied. The development of our knowledge of metabolism is even more recent and incomplete. Some of the processes involving food utilization and energy production are emerging into focus, but as yet only the barest beginning has been made in finding out what chemical reactions occur during the normal functioning of living things.

Biochemical research is being intensively pursued in hundreds of laboratories throughout the world. The methods of study are drawn mainly from the older sciences such as chemistry, physics, mathematics, biology, physiology, etc., of which biochemistry is an outgrowth and descendant.

Isolation Methods. Efforts to ascertain the chemical nature of biological materials ordinarily start with an extraction or purification process by which one constituent is *isolated, i.e.*, separated in pure form from all the others. The isolation of a pure biological substance is often a difficult feat because most biological materials are complex mixtures containing hundreds of different individual chemical substances, many of which frequently are closely similar in composition or properties and, therefore, difficult to separate. In addition, the particular substance sought may be present in very low concentrations, perhaps only one part in many million parts of the source material. For example, Doisy and co-workers extracted and processed the equivalent of four tons of sow ovaries to obtain about 10 mg. of the sex hormone, estradiol (p. 292). This small yield represented about half of the hormone originally present, since its normal concentration in the ovary of the sow is only one part in 150,000,000! This isolation of estradiol represents an achievement on a par with the famous work of the Curies in obtaining radium from pitchblende and illustrates some of the difficulties which confront the biochemical investigator studying the composition of living things.

There are many kinds of procedure used in isolating biochemical substances, and only a brief indication of their nature can be attempted

here. Frequently large classes of substances can be separated from each other because of their different degrees of solubility. For example, a mixture of fat and sugar can easily be separated by shaking with ether and water. These two solvents, being immiscible, on standing form layers, one of which contains the sugar and the other the fat. Two types of materials both dissolved in the same solvent may be separated by causing one to precipitate. For example, a boiling water extract of a fresh fruit or vegetable will contain, among other things, both sugars and proteins. This mixture can be separated by adding a soluble salt of a heavy metal such as lead acetate and filtering, since the proteins are thereby rendered insoluble. Again, some substances are held on the surface of *adsorbents, e.g.*, activated charcoal, while others are not; certain substances can be volatilized (distilled) leaving others behind. By progressively applying such *fractionation procedures*, a particular substance can be gradually separated from the compounds which are originally mixed with it in the living material, and thus brought nearer to a state of purity.

Once an individual chemical substance has been isolated, it can be analyzed by standard chemical methods, broken down into simpler fragments, which are also analyzed, and in general examined to see just how it is constituted chemically. If the compound is not of too great complexity, *e.g.*, has a molecular weight of a few hundred or less, its structure is usually established within a few years. The results of this work are expressed as a *structural formula*, which shows just what the substance is and how it may be expected to react with other substances. Since most compounds isolated from living things are organic (carbon) compounds, such studies fall into the realm of *organic chemistry*.

Nutrition. A large part of biochemical research for the past fifty years has been concerned with the *nutrition* of animals, plants, and microorganisms. The objectives of this work have been to find out just what chemical substances are needed in the food of living organisms to nourish them properly and to determine what purpose each nutrient serves. In the earlier days of the twentieth century, attention was focused mainly on the energy-yielding and body-building materials which constitute the bulk of the food, namely the carbohydrates, fats and proteins. More recently, substances required in smaller amounts such as the mineral elements, vitamins, and other growth factors have been intensively studied. These remarks apply particularly to animals and microorganisms, as plants need only mineral elements besides carbon dioxide and water for nourishment.

The experimental methods of investigating these questions are similar in principle regardless of the type of organism being studied, and may be illustrated for the case of animals. The general approach has been to feed animals a diet prepared from purified ingredients and to observe

whether they grew normally and remained healthy. Usually growth declined, but by supplementing the purified diet with some natural food material, such as yeast, whole milk, or liver extract, growth was restored. Such experiments showed that the supplement must have contained some essential food factor lacking from the purified experimental (basal) diet. The next step was to isolate this substance, determine its chemical structure, and add it as a pure compound to the basal diet for further feeding trials. Whenever this was done, it usually was found that extra supplements were again needed, or in other words, that the supplement first used must have been contributing more than one essential food factor.

By such methods it has now been shown that a long list of chemical substances is required to fulfill the dietary needs of animals. In the case of rats and chickens most, if not all, of the essential food factors have been discovered, since rapid growth and apparently normal development can be obtained on diets composed exclusively of pure chemicals. However, when such a "synthetic diet" is fed to other animals such as guinea pigs, they respond so poorly that other still-unknown food substances are obviously needed. In fact the use of many different species of animals for nutritional studies has been a fruitful source of information, for, although many requirements are similar, many differences have also been found. Not only animals, but plants and microorganisms have been extensively studied as to their nutritional requirements, and the latter especially, because of their small size and rapid growth, have served as admirable test subjects.

Study of Metabolic Reactions. The study of the chemical reactions that take place in living organisms is regarded by many biochemists as the most significant and fundamental aspect of the science. As pointed out above, relatively little progress along this line was made until recently, but since emphasis is now shifting strongly in this direction, the rate of discovery of new information has sharply increased, and extensive additions to our knowledge may be expected in the relatively near future. In studying metabolic reactions one approach has been to investigate the composition of the food consumed and the waste eliminated by an organism in order to attempt to deduce what must have happened inside the organism to convert the one into the other. This method has yielded some information, but obviously suffers from severe limitations.

A more fruitful approach has been to transfer the reactions being studied from the organism to the test tube. In several instances it has been possible to duplicate cellular reactions in the absence of the cells themselves. For example, many of the intermediates, such as succinic acid, involved in carbohydrate metabolism are oxidized by molecular oxygen to carbon dioxide and water when added to suitable tissue preparations. Finely ground suspensions of liver tissue in an aqueous buffer are suitable for this purpose. Similarly, cell-free yeast preparations can ferment glucose to carbon dioxide and alcohol. Once such a

system that is able to reproduce typical metabolic reactions *in vitro* [1] is discovered, the way will be open for experimental study. The chemical compounds involved in each step of the process can be isolated in pure form, and the effect of removing them from the system or replacing them at various concentrations can be observed. The catalysts (enzymes and coenzymes) which make the whole process possible can similarly be studied one at a time, and, in general, each step can be subjected to detailed examination. It is in this way that much of our knowledge of metabolism has been acquired.

A still newer technique, which promises to be of major significance in unraveling the chemistry of metabolism, is based on the use of isotopes. The widespread use of this method was made possible by the atomic energy development. Eventually, this may well prove to have been one of the most constructive and valuable results of that program. Isotopes of the common elements—C, H, O, N, S, P, and others—are used as metabolic "tracers" by incorporating one or more of them into some substance normally involved in metabolism. The "labeled" metabolite is then administered to the test organism. After a suitable interval the distribution of the isotope in the various tissues or tissue components of the organism is determined. Thus if a rat is fed glycine containing N^{15} in the amino group, and the purine compounds in the animal's tissues are later found to contain N^{15} in comparable amounts, it may be concluded that glycine is concerned in the biosynthesis of purines, and specifically that one of the nitrogen atoms in the purine ring came from the amino group of glycine. Other examples of the use of isotopes will be encountered throughout the text.

Information about metabolic processes can also be obtained by blocking some particular process and then searching for a way to remove the block. The desired effect can be obtained, for example, with antimetabolites, substances so similar to certain normal metabolites that they get in the way of the latter but yet are unable to carry out their functions. Again, it is often possible to produce mutants of lower organisms (*e.g.*, the mold, *Neurospora*), which lack the power to carry out certain metabolic reactions. In such cases it has frequently been observed that the effect (*e.g.*, growth failure) of the block may be removed by administering some apparently unrelated chemical. This indicates that the counteracting agent may be the substance normally formed by the blocked reaction. As an illustration, suppose an organism needs substance *A* to serve as a catalyst for the transformation of *B* into *C*:

$$B \xrightarrow{A} C$$

An antimetabolite of *A* would probably inhibit the growth of this organism, but this inhibition would be counteracted by *C*.

[1] *In vitro* means, literally, in glass and implies occurring outside any living thing.

Relation of biochemistry to biology

Biologists have traditionally studied living organisms on the basis of the *cell,* as the smallest intact living unit. The cell occupies much the same relative position in biology as the molecule does in chemistry. The smaller components of living cells have come under scrutiny, as the biologist, equipped with ever more powerful microscopes, has probed deeper and deeper into the mysteries of living matter. The main parts of a typical cell are the *cell wall, nucleus,* and *cytoplasm.* The living material making up the nucleus and cytoplasm is termed *protoplasm;* it is a grayish, translucent, jelly-like material, which under the microscope can be seen to consist of a meshwork filled with fluid. The nucleus contains *chromosomes,* and these in turn, under very high magnification, reveal structural irregularities which may have functional significance. Thus the biologist studies and interprets life mostly in terms of its smallest *visible* fragments.

From the chemical viewpoint, protoplasm is an aqueous, colloidal solution containing protein as the chief solid ingredient, but with appreciable amounts of fatty substances, nucleic acids, and other compounds present. The metabolic reactions occurring in the cell take place in this solution, and are studied and interpreted by the biochemist in terms of *molecules* of the reacting substances. Most molecules are far too small to be seen in any microscope, and their actual existence can only be surmised from indirect evidence. However, the giant molecules of proteins and nucleic acids are large enough so that they can actually be "seen," that is, photographed, with the help of the electron microscope, an instrument that makes possible 50,000–100,000 fold magnification.

It seems most probable that the merging of biochemistry and biology will continue in the future to an even greater extent, as the functional activities of living things come more to be studied and explained in chemical terms. However, it will not suffice to regard metabolism merely as a group of chemical processes occurring at random in the same solution. Each living cell is a miniature "chemical factory" where food molecules pass in an orderly fashion through a long series of interrelated chemical reactions. A highly organized physical structure, with each catalyst (enzyme) in a definite position in relation to the others, must exist to accomplish this end. The study of such levels of organization can probably be more properly classified as biology rather than as biochemistry, although it must be obvious that the borderline is indefinite.

Study of biochemistry

The first task of the beginning student must be to learn something of the materials of the cell in order to provide a basis for subsequent

study of metabolic processes. At least an elementary knowledge is needed, not only of the major cellular components (water, carbohydrates, fats, and proteins), but also of the minerals, vitamins, hormones, and enzymes, which, although present in smaller amounts, are equally vital to the living organism.

Relatively little time can be devoted, at first, to discussion of detailed evidence for various facts and how this evidence was obtained, since major emphasis must be given to the facts themselves. In other words, the *results* rather than the *methods* of biochemical research form the chief subject matter of the beginning course. It is for this reason that the methods have been briefly outlined in this introductory chapter. As in all elementary studies, the student is asked to accept great masses of information more or less on faith, with the clear understanding, however, that each fact is firmly supported by experimental evidence which he can review and assess for himself, if he so desires. References and suggested readings are listed at the end of each chapter for this purpose.

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Chapter 2

WATER

Occurrence and importance

Water is the most abundant substance in living matter. The great physiologist, Claude Bernard, said, "All living matter lives in water." In his *Outline of History*, Wells put it this way, "We talk of breathing air, but what all living beings really do is to breathe oxygen dissolved in water."

Table 2–1 gives the water content of some typical animal, plant, and microbial materials. The human body is about 65 per cent water, a corn plant about 75 per cent, and a bacterial cell about 80 per cent. The amount of water varies not only with the type of material but also with its period of development. Two examples, for which we have adequate data, will show the variation with age. The pig embryo at 15 days of development consists of 97 per cent water and 3 per cent solids, and at birth the young pig is made up of about 89 per cent water and 11 per cent solids. The water content continues to decrease as the pig grows, being about 67 per cent at 100 lbs. weight and 43 per cent for a very fat animal weighing 300 lbs. The same relationship between water content and age holds for other farm animals and also for man.

The water content of the corn plant remains practically constant, about 88 per cent, during the actively growing period from the seedling to the tassel state, decreases rapidly to around 70 per cent at the time the kernels begin to glaze, and falls to about 52 per cent when the plant is mature and ready to harvest.

A high water content is characteristic of youth and activity and a lowered figure is associated with old age and inactivity. The relation between water content and activity of tissues is further demonstrated by comparison of different tissues in the same individual. The metabolically active tissues of the body, *e.g.*, brain and liver, contain much more water than the relatively inactive portions such as bones and fatty tissues.

Table 2–1

Water content of some important biological materials

Material	*Water* [per cent]
Human body	65
Brain, gray matter	84
Liver	76
Muscle	73
Blood	80
Milk	87
Saliva	99.5
Bone	10–40
Adipose tissue (mainly fat)	10–30
Larvae of clothes moth	58
Pig embryo, 15 days old	97
Pig at birth	89
Pig at maturity, depending on fatness	40–50
Corn plant, seedling to tassel period	85–90
Corn plant, kernels glazed	68–72
Corn plant, maturity	50–60
Bacteria	73–90
Yeasts	68–83
Molds	75–85

It is all too common a fallacy to limit the meaning of "foods" to the energy-yielding materials—carbohydrates, fats, and proteins—with the inclusion perhaps of mineral elements. If the term food be considered to include all substances that are essential for the growth and repair of body tissue, as most certainly it should, then water likewise is truly a food. This error in thinking has arisen from the fact that in the past most biologists have treated water as if it were an inert material and have looked upon the solids of plant and animal tissues as the important part of the organism. Gortner has pointed out how mistaken is this view; he illustrates his argument by citing the composition of the tadpole, 95 per cent water and 5 per cent solids. "It would be ridiculous to speak of this organism as being composed of only 5 per cent of vital materials. The water is as much a part of the tadpole as are the fats, proteins, etc., which serve to form the gel structure, and the biochemical and biophysical reactions which take place within the cells and tissues of the tadpole are determined probably more by the water which is present than by any or all of the other constituents."

Free and bound water

The term "bound water" has come into use to designate water that has been adsorbed by the colloids of the living cell, in contrast to "free water,"

which is not an integral part of the plant or animal tissue with which it is associated. The major part of bound water is held probably by proteins, but other classes of compounds are known to retain relatively large amounts of water. Thus adipose tissue contains considerable water, certain of the compound lipides, such as lecithin, emulsify readily in water, and the polysaccharides of plant tissues are decidedly hydrophilic.

It is not certain just how bound water is held by colloidal material. One explanation applied to proteins is that sharing of electrons between the protein molecule and the water molecule sets up a binding force that holds the water to the protein. Such a force is called a hydrogen bond or bridge and consists of an electropositive hydrogen atom standing between two electronegative atoms, *e.g.*, N and O, thus —N : H : O—. The hydrogen shares its electron with both the N and O.

Proteins contain many groups such as $—NH_2$, —COOH that can form a hydrogen bond with water. A protein molecule may contain several thousand binding groups. For example, gelatin, a rather small protein having a molecular weight of about 35,000, is calculated to have 960 molecules of water bound to each molecule of gelatin when a gel is formed. There is much difference of opinion as to the quantity of water held by proteins in solution, but 0.3 g. of water per gram of protein is a commonly suggested figure.

Bound water, especially that bound by the protoplasm of the cell, appears to be one of the several important factors involved in frost and drought resistance. Plants that are exposed to low temperatures in winter increase the proportion of bound water and the concentration of water-soluble protein in the cell sap, thus developing what is called winter hardiness. Plants, such as cactus, that live under arid or semi-arid conditions hold their water largely in the bound state. Insects also increase the percentage of bound water under conditions of cold or drought.

Yeast cells furnish another example of the intimate association of residual water and life processes. A commercial product known as active dry yeast contains only about 8 per cent moisture, but the cells are still alive and will survive for many months. If soaked in warm water for a few minutes, the yeast promptly starts producing carbon dioxide and can be used in place of baker's press yeast for bread-making. However, if the cells are dried to around 5 per cent moisture, they die, and will not revive when placed in water.

On the other hand, cultures of most microorganisms if lyophilized (dried from the frozen state) can be kept in this condition for years and still grow when placed in a suitable medium.

Necessity for water

The demands of the body for water are far more imperative than those for food. An animal can live for 100 days or more without food but dies within five to ten days if no water is supplied. With a Scotch collie, Hawk conducted two experiments in which the dog was maintained for 105 and 117 days, respectively, without food, but with an abundance of water. At the end of each period the animal was still in a fair condition of health.

In the life of the plant enormous quantities of water are transpired. From three hundred to four hundred pounds of water are involved in the manufacture of one pound of dry matter. Water is one of the great raw materials from which the plant produces sugars, fats, proteins, and all the other substances which go to make up the plant cell.

Function of water

Since all chemical changes involved in digestion are of a hydrolytic nature, water is concerned in the first step toward utilization of fats, proteins, and the higher carbohydrates. Water functions as a medium for the transportation of food materials during digestion, absorption, and circulation; and of waste products, as well, in the process of elimination. Hawk has demonstrated that digestion by saliva is more rapid if the saliva is diluted with about seven times its volume of water. Gastric digestion and pancreatic digestion also are aided by liberal quantities of water. Carbohydrates, fats, and proteins are more completely absorbed when large quantities of water are ingested with the food. The growth of bacteria, and consequent putrefactive processes, are decreased by the use of liberal quantities of water with food.

Water also plays an important role as a heat regulator. Because of the high specific heat of water, oxidation in the body can proceed without greatly increasing the temperature at the site of oxidation. Water is a good conductor of heat and thus aids in the transfer of heat from the interior to the surface of the body. Finally, because of its high latent heat of vaporization, water carries off heat by vaporization in the expired breath and evaporation from the surface of the body. It is estimated that about 25 per cent of the heat produced in the body is carried off by way of the breath and by evaporation from the skin. In animals that do not perspire freely—dogs, swine, cattle—excess heat is dissipated by increasing the respiration (panting).

Finally, water performs an important function as a lubricant in the many movements of the muscles, joints and organs of the body.

Water requirement

The water requirement varies with different conditions. For an adult doing no manual work, and at the time of year when the weather does not induce visible perspiration, it is estimated that an intake of about 3 l. of water per day is needed for good health. Of this quantity, about 2 l. will be contained in the food, leaving 1 l. to be drunk as water. Many health authorities advocate drinking from 5 to 8 glasses of water daily, which is more than most people manage to do.

Individuals who work under conditions which induce much perspiration, for example, blast furnace workers, may lose many liters of sweat per day and hence must drink large quantities of water. Since the sweat carries with it salts, depletion must be avoided by taking salt tablets or by adding salt to the drinking water. About 0.1 per cent of sodium chloride in the water is scarcely perceptible, and such water quenches thirst about as well as unsalted water.

The water requirement would be even higher than it is except for the fact that the ingested water is reused several times for different purposes before it is finally lost from the body. Water withdrawn from the blood stream for such secretions as saliva, gastric juice, pancreatic juice, intestinal juice, and bile is salvaged during absorption and made available for further use. The volume of these secretions amounts to from 3.7 to 9.8 l. daily, which means an average reuse of two to three times.

Formally it was thought that water should not be drunk with meals, but as a result of Hawk's work it appears that this idea is erroneous. Under certain conditions such as dropsy, heart and kidney disturbances large quantities of water may be objectionable, but for the normal individual it is probable that too little water is usually consumed.

Metabolic water

Water is invariably one of the end products of oxidation of carbohydrates, fats, and proteins. Such water is called "metabolic water." To be specific, let us refer to the equation for complete oxidation of glucose in the body:

$$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O + 683\ \text{Cal.}^1$$

During oxidation of 180 g. (1 mole) of glucose, 108 g. (6 moles) of water is produced with accompanying liberation of 683 Cal. of heat. By the same proportion, 15.9 g. of water would be formed for every 100 Cal. derived by oxidation of glucose.

[1] For a definition of *calorie* see p. 413.

From fats, proteins, and starch the yield of water per 100 Cal. is somewhat less than the amount calculated for glucose. Approximately 12.5 ml. of metabolic water is formed during oxidation of a 100 Cal. portion of a diet in which proteins, fats, and carbohydrates contribute 15, 35, and 50 per cent, respectively, of the total calories. On this basis, a person consuming 3000 Cal. daily would derive 375 ml. of water from oxidation of these energy-yielding foods, an amount approximating one-tenth of the intake of water as a drink.

Some species of insect, *e.g.*, clothes moth and grain weevil, obtain nearly all of their water from metabolic processes. The clothes moth feeds on wool, which contains about 5–10 per cent of absorbed water. For each gram of dry wool (protein) consumed, approximately 0.4 ml. of water is formed by the chemical processes involved in metabolism.

Water balance

For a normal man the intake and output of water are so regulated that the amount in the body remains fairly constant. If the intake is increased without any other change in external conditions, the output in the urine is very promptly increased. If the atmospheric temperature rises, or if muscular effort is increased, then more water is eliminated through the skin as insensible or sensible (visible) perspiration and less is put out in the urine. With increased muscular effort there is also more water eliminated through the lungs, but the greatest variation occurs in the volume of urine and perspiration. A typical water balance for an average-sized man of sedentary occupation is about as follows:

Water intake	ml.	*Water output*	ml.
Drinking water	850	In urine	1450
Water in coffee, milk, soup, and other fluids	600	In feces	150
Water in solid foods	700	Evaporated from the skin	600
Metabolic water	350	Vaporized through the lungs	350
Total:	2500		2550

On this particular day there is a negative balance of 50 ml.; on a succeeding day the balance might be positive by that much or more.

Water supplies

The importance of a pure water supply cannot be overestimated. To determine the potability of a water requires careful chemical and bacteriological analyses. Pure water in the chemist's sense of the term is not required to furnish a sanitary water supply. All ground and surface waters dissolve more or less salts and other materials. It is only when

such waters contain harmful organisms or acquire offensive odors or tastes that they become objectionable. A good drinking water should be clear, colorless, odorless, have a cool and refreshing taste, and be free from harmful organisms.

In the chemical examination of water the different forms of nitrogen are regarded as the best index of the quality of the water. The water is analyzed for its content of albuminoid ammonia, ammonia, nitrites, and nitrates. These different forms of nitrogen are closely related to one another. The albuminoid ammonia really represents protein nitrogen and is readily converted by organisms into ammonia. Other organisms then oxidize the ammonia to nitrites and nitrates. The nitrogen of the nitrates may then be utilized by plants that grow in the water and be again built up into proteins. These processes are called ammonification and nitrification and form a part of what is known as the nitrogen cycle in nature. The relation of the different forms of nitrogen may be expressed by the following equations in which glycine is taken to represent protein:

Ammonification:

$$2CH_2NH_2COOH + 3O_2 = 2NH_3 + 4CO_2 + 2H_2O$$

Nitrification:

$$2NH_3 + 3O_2 = 2HNO_2 + 2H_2O$$

$$2HNO_2 + O_2 = 2HNO_3$$

$$2HNO_3 + CaCO_3 = Ca(NO_3)_2 + H_2O + CO_2$$

These compounds of nitrogen are not toxic in the quantities in which they occur in water. Far more ammonia, for example, is produced as a result of metabolism than is consumed in the drinking of water. However, the presence of a constant and continuing supply of albuminoid ammonia, ammonia, and nitrates may indicate that the water is being contaminated by sewage, since these forms of nitrogen are particularly high in sewage. A state of change is regarded as a state of danger and calls for careful investigation as to the origin of these forms of nitrogen. Care must be observed in interpreting the data obtained by analyzing water. The normal nitrogen content of such waters must be known before judgment can be passed. Deep well water would not have the same nitrogen content as a surface or spring water. It is necessary to know something of the topographical features surrounding the water supply.

The chloride content of water is often also of value in determining the character of the water. If it has been polluted by sewage, the chloride content will be abnormally high. Here again, however, it is necessary to observe great caution in passing judgment. Waters from along the coast or from regions where salt deposits exist may be very high in chlorides and still be perfectly safe. It is not the absolute amount, but

the departure from the normal in that vicinity that is significant. Sewage, which contains a very high content of salt, will raise the chlorine content very quickly if a little of it gets into the water.

Although sedimentation, flocculation with chemicals, and filtration through layers of sand and gravel remove much suspended matter and hence lessen the bacterial content of water, these methods alone cannot be relied upon for purification of a public water supply. The agent most commonly employed to destroy bacteria in water is liquid chlorine. Penfield and Cushing state that 85 per cent of the public water supplies of the United States are sterilized with chlorine. According to these authors the average typhoid death rate in 77 important cities of the United States has decreased from 20.54 deaths per 100,000 in 1910 (when the use of chlorine was initiated) to only 0.76 in 1937. Better water supplies, and the use of sulfa drugs, antibiotics, and other therapeutic measures, have decreased the typhoid death rate to 0.2 per 100,000 in 1948.

Hardness of water

From the household and industrial viewpoint, the hardness of water is an economic question that involves the cost of large quantities of soap and water-softening materials. The hardness of water is due to the presence of bicarbonates, sulfates, chlorides, and silicates of calcium, magnesium, and iron. These salts form insoluble precipitates with soap and therefore give what is called hardness to the water. New types of cleaning agents, called "synthetic detergents" (p. 87), have been developed in recent years. They form soluble calcium and magnesium soaps and hence can be used in hard water.

Hardness of water is spoken of as being temporary or permanent depending upon whether it is due to bicarbonates or other salts. If the hardness is due to bicarbonates, heating or boiling the water will, to a large extent, precipitate the calcium or magnesium bicarbonates as insoluble carbonates. On the other hand, boiling has no effect upon water that contains sulfates or other salts of calcium and magnesium. Such waters are said to be permanently hard. Many different methods for softening hard water can be used such as boiling, or addition of lime, washing soda, phosphates, or other precipitants. In all cases a precipitation of the calcium and magnesium is the end to be desired. The action of these precipitants may be represented by the following equations:

Heat:

$$Ca(HCO_3)_2 = CaCO_3 + H_2O + CO_2$$

Lime:

$$Ca(HCO_3)_2 + Ca(OH)_2 = 2CaCO_3 + 2H_2O$$

Washing soda:

$$Ca(HCO_3)_2 + Na_2CO_3 = CaCO_3 + 2NaHCO_3$$
$$CaSO_4 + Na_2CO_3 = CaCO_3 + Na_2SO_4$$

Phosphates:

$$3Ca(HCO_3)_2 + 2Na_3PO_4 = Ca_3(PO_4)_2 + 6NaHCO_3$$
$$3CaSO_4 + 2Na_3PO_4 = Ca_3(PO_4)_2 + 3Na_2SO_4$$

The use of various water-softening materials in the kitchen and laundry of the average household is not a very satisfactory procedure. In most cases little or no softening of the water, and consequent saving of soap, is effected. At best it is a temporary expedient and to a large extent means waste of money. A satisfactory method of softening water is by means of a zeolite. Silicates of this character are sold under such trade names as Permutit, Refinite, and Bormite. Water treated in this way is soft. In fact, it requires less soap than distilled water because of the presence of a small amount of sodium bicarbonate. The softening of water by means of a silicate may be represented by the following equation:

$$Ca(HCO_3)_2 + Na_2O{\cdot}Al_2O_3{\cdot}2SiO_2{\cdot}6H_2O =$$
$$CaO{\cdot}Al_2O_3{\cdot}2SiO_2{\cdot}6H_2O + 2NaHCO_3$$

After a time the silicate will have taken up all the calcium or magnesium that it will hold and must then be regenerated if the water is to be softened. This is done by means of a strong solution of salt that displaces the absorbed calcium or magnesium and again forms the sodium silicate. This operation is called the regeneration of the silicate and is indicated by the following equation:

$$CaO{\cdot}Al_2O_3{\cdot}2SiO_2{\cdot}6H_2O + 2NaCl = Na_2O{\cdot}Al_2O_3{\cdot}2SiO_2{\cdot}6H_2O + CaCl_2$$

A more recent method for softening water is by means of cation exchange resins. Such resins are extremely insoluble, high polymer organic compounds that contain many acidic groups, *e.g.*, sulfonic, $—SO_3H$; carboxyl, —COOH; etc. A phenol sulfonic acid resin is made by polymerizing *m*-phenol sulfonic acid, $C_6H_4(OH)SO_3H$, and formaldehyde. Commercial products of this type are Amberlite IR-100 and Dowex-50. The removal of a cation such as Ca^{++} from water by the resin may be represented by the following equation:

$$Ca(HCO_3)_2 \quad \text{or} \quad CaSO_4 + 2NaR = CaR_2 + 2NaHCO_3 \quad \text{or} \quad Na_2SO_4$$

In the above equation NaR represents the sodium form of the ion exchange resin. Similar equations can be set up to show the removal of magnesium, iron, and other cations. When the resin becomes loaded with cations, it is regenerated by washing with sodium chloride brine. The reaction is illustrated by the equation

$$CaR_2 + 2NaCl = 2NaR + CaCl_2$$

An ion exchange resin that removes anions can be synthesized by condensing a phenol amine, *e.g.*, $C_6H_4(OH)CH_2NHCH_3$ and formaldehyde. Amberlite IR4B is a commercial product of this type. The removal of anions may be represented by the equation

$$CaSO_4 + 2ROH = Ca(OH)_2 + R_2SO_4$$

The alkalinity thus produced may be neutralized by using the anion exchanger in series with an acid form of cation exchanger (HR), in which case the water is completely demineralized, thus

$$Ca(OH)_2 + 2HR = CaR_2 + 2H_2O$$

The anion exchanger can be regenerated with sodium hydroxide, and the cation exchanger with sulfuric acid.

A desalting kit for the production of potable water in case of forced landings in overseas flying consists of silver zeolites (AgZ), silver oxide, and barium hydroxide compressed into briquets and placed in a suitable container for filtering sea water. The reactions involved are as follows:

$$AgZ + NaCl = NaZ + AgCl$$

$$Ba(OH)_2 + MgSO_4 = Mg(OH)_2 + BaSO_4$$

The sodium, chloride, magnesium, and sulfate ions, the chief constituents of sea water, are removed as the insoluble compounds NaZ, AgCl, $Mg(OH)_2$, and $BaSO_4$. The capacity of the zeolite material is about ten times its volume of sea water.

The above discussion of ion exchangers is merely a bare outline of the subject, and the interested student is referred to the books listed at the end of the chapter for complete information on this complex and rapidly developing field of work.

REVIEW QUESTIONS ON WATER

1. Would you expect the young leaves of a growing plant to be higher or lower in water content than the fully developed leaves? Explain.
2. Arrange these materials in ascending order of water content: milk, blood, cabbage, saliva, strawberries, fish. (Consult Tables 2–1 and A–1.)
3. Explain the terms "bound water" and "free water."
4. Explain the term hydrogen bond. With which other elements is it associated? Consult the index.
5. What changes in composition would you expect to find in wheat plants analyzed in September and again in December?
6. What is the daily water requirement of an adult? Name some of the chief functions of water in the body.
7. Explain how clothes moth larvae get their water. Can you name another insect or living organism that gets its water in the same way?
8. What is meant by "metabolic water"? What is the approximate contribution of this water to the total intake?

9. Discuss the advisability of drinking liberal quantities of water at meal time.
10. Write an equation for the reaction between soap and hard water.
11. Write an equation for the softening of water by zeolites (silicates).
12. Explain the terms (1) temporary and (2) permanent hardness of water.
13. Define the term ion exchange resin. Find the name of one resin other than those given in the text and the name of the company that produces it.
14. Write equations for the removal of $MgCl_2$ from water by ion exchange resin.

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Chapter 3

CARBOHYDRATES

Composition and definition

The word "carbohydrate" literally means carbon combined with water and originates in the fact that many carbohydrates have the composition $C_x(H_2O)_y$. The values of x and y may range from three to many thousand. Although several carbohydrates do not have this composition, and some other substances do, *e.g.*, lactic acid ($C_3H_6O_3$), the term nevertheless fits the great majority of carbohydrates and is in common use.

Carbohydrates may be chemically defined as simple sugars, or more complex substances which yield simple sugars on hydrolysis.[1] Simple sugars are either aldehydes or ketones which contain at least two, and usually several, hydroxyl groups. The aldehyde-alcohol type is called an *aldose, e.g., glucose,* and the ketone-alcohol type a *ketose, e.g., fructose.*

Occurrence and importance

The plant world is the great source of the carbohydrates. The dry matter of plants (excepting certain oily seeds) is from 60 to 90 per cent carbohydrate. These compounds are constituents of most materials that satisfy the primary needs of human life.

Our *food* is made up principally of carbohydrates—approximately 70 per cent by weight of the food in the average diet. Much of our *clothing* is made from carbohydrates—cotton, rayon, and linen. In the United States probably more *houses* are built of wood than of all other materials combined. Even in many buildings of brick and stone, wood enters into the construction of walls, floors, stairways, and windows. The great *fuel materials,* wood and coal, are either carbohydrates or derived from carbohydrates. The carbohydrates are at the very foundation of the economic structure of society.

The importance of the carbohydrates is shown by Table 3–1. The carbohydrate industries listed employ nearly as many people and turn out products of greater value than the combined machinery and chemical and drug industries.

[1] Hydrolysis consists in the cleavage of a complex molecule into smaller fragments with the simultaneous addition of water.

Table 3–1

Economic importance of some industries based on carbohydrates *

Industry	*Wage earners*	*Value of products shipped*
1. Lumber and products (except furniture)	635,708	$4,691,931,000
2. Cotton and rayon fabrics, yarns, threads	604,469	5,496,299,000
3. Grain mill and bakery products	392,585	8,183,849,000
4. Paper and products	449,833	7,051,485,000
5. Confectionery	75,165	944,925,000
6. Sugar (cane and beet)	35,423	1,141,437,000
7. Starch, dextrin, sirups	12,324	459,978,000
8. Fermentation products (beverages, vinegar, yeast, etc.)	91,754	1,671,712,000
9. Canvas products and textile bags	24,453	447,089,000
10. Cordage and twine	15,950	167,648,000
	2,337,664	$30,256,353,000

* Compiled from the 1947 *Census of Manufacturers*, Bureau of the Census, 1950, and from the *Statistical Abstract of the United States, 1951*, published by the Department of Commerce.

For comparison, figures for some other industries from the same source, for the same year, are as follows:

Industry	*Wage earners*	*Value of products shipped*
Machinery, including electrical	2,346,682	$19,667,327,000
Industrial chemicals, and drugs	353,445	5,145,963,000

An abridged classification of carbohydrates

I. Monosaccharides
  A. Trioses, $C_3H_6O_3$
    1. Aldotriose: D-*glyceraldehyde*
    2. Ketotriose: *dihydroxyacetone*
  B. Tetroses, $C_4H_8O_4$
    1. Aldotetroses: D-*erythrose*, D-*threose*
  C. Pentoses
    1. Aldopentoses, $C_5H_{10}O_5$: L-*arabinose*, D-*arabinose*, D-*xylose*, D-*ribose*
    2. Ketopentose, $C_5H_{10}O_5$: L-*xylulose*
    3. Desoxypentose,[1] $C_5H_{10}O_4$: 2-*desoxy*-D-*ribose* (*desoxyribose*)
  D. Hexoses
    1. Aldohexoses, $C_6H_{12}O_6$: D-*glucose*, D-*galactose*, D-*mannose*
    2. Ketohexoses, $C_6H_{12}O_6$: D-*fructose*, L-*sorbose*
    3. Desoxyhexoses, $C_6H_{12}O_5$: 6-*desoxy*-L-*mannose* (L-*rhamnose*), 6-*desoxy*-L-*galactose* (L-*fucose*)
    4. Aminohexoses, $C_6H_{13}O_5N$: 2-*amino*-D-*glucose* (D-*glucosamine*), 2-*amino*-D-*galactose* (*galactosamine*)

[1] The prefix "desoxy" means "lacking oxygen." Note that the formula of the desoxypentose is $C_5H_{10}O_4$, whereas the other pentoses are $C_5H_{10}O_5$.

5. Hexuronic acids, $C_6H_{10}O_7$: D-*glucuronic acid*, D-*mannuronic acid*, D-*galacturonic acid*

E. Heptoses

1. Ketoheptoses, $C_7H_{14}O_7$: D-*mannoheptulose, sedoheptulose*

II. Disaccharides, $C_{12}H_{22}O_{11}$

A. Anhydrides[1] of glucose and galactose: *lactose, melibiose*

B. Anhydride of glucose and fructose: *sucrose*

C. Anhydrides of glucose and glucose: *maltose*, iso-*maltose, cellobiose, gentiobiose, trehalose*

D. Anhydrides of a hexose and a hexuronic acid (aldobiuronic acids): *cellobiuronic acid, gentiobiuronic acid*

III. Trisaccharides, $C_{18}H_{32}O_{16}$

A. Anhydride of galactose, glucose, and fructose: *raffinose*

B. Anhydride of glucose, fructose, and glucose: *melizitose*

IV. Polysaccharides

A. Homopolysaccharides (anhydrides of single monosaccharides)

1. Pentosans, $(C_5H_8O_4)_x$: *xylan, araban*

2. Hexosans

a. Glucosans, $(C_6H_{10}O_5)_x$: *cellulose, starch, dextrin, glycogen, bacterial dextran.*

b. Fructosans, $(C_6H_{10}O_5)_x$: *inulin, bacterial levan*

c. Galactosans, $(C_6H_{10}O_5)_x$: *snail galactogen*

d. Mannosans, $(C_6H_{10}O_5)_x$: *vegetable nut mannan, salep mannan*

e. Polyglucosamine:[2] *chitin*

f. Polyuronides,[3] $(C_6H_8O_6)_x$

(1) Polygalacturonic acid: *pectic acid*

(2) Polymannuronic acid: *alginic acid*

B. Heteropolysaccharides (anhydrides of several monosaccharides)

1. Hemicelluloses: alkali-soluble polysaccharides associated with cellulose in wood, straw, cornstalks, and other fibrous plant tissues. On hydrolysis, form mainly D-xylose, together with L-arabinose, D-glucose, uronic acids, and other sugars.

2. Plant gums: gums from injured trees or bushes, mostly water-soluble, and forming D-glucuronic acid and other sugars on hydrolysis. Examples: *gum arabic, mesquite gum, cherry gum.*

3. Plant mucilages: polysaccharides extractable from the seeds, roots, leaves, and bark of various plants, forming colloidal solutions. Examples: *gum gatto, linseed mucilage, agar-agar.*

4. Mucopolysaccharides: water-soluble polysaccharides found in animals and often associated with protein. Usually form aminohexoses and (or) hexuronic acids, as well as other sugars when hydrolyzed. Examples: *hyaluronic acid, heparin, chondroitin sulfate, pneumococcus polysaccharides, blood-group polysaccharides.*

V. Substances Related to Carbohydrates

A. Sugar alcohols, open chain

1. Four carbon type, $C_4H_{10}O_4$: *erythritol*

2. Five carbon type, $C_5H_{12}O_5$: *xylitol, arabitol, ribitol*

3. Six carbon type, (hexitols), $C_6H_{14}O_6$: *mannitol, sorbitol, dulcitol*

[1] An anhydride is a product formed by removing the elements of water from another substance or substances. Frequently an H atom is split out of one molecule and an OH group from another, and the residues unite to form the anhydride.

[2] Polysaccharide giving glucosamine and acetic acid on hydrolysis.

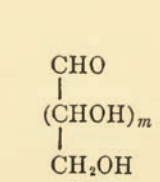
[3] Polysaccharide giving a uronic acid on hydrolysis.

B. Cyclic polyalcohols: *inositol*
C. Sugar acids (other than uronic acids)
1. Aldonic acids, $C_6H_{12}O_7$: D-*gluconic acid*, D-*mannonic acid*, D-*galactonic acid*.
2. Saccharic acids, $C_6H_{10}O_8$: *mucic acid*, *saccharic acid*.
3. Ketoaldonic acids, $C_6H_{10}O_7$: 2-*Ketogluconic acid*, 5-*ketogluconic acid*.
4. Ascorbic acids, $C_6H_{10}O_6$: *ascorbic acid*.

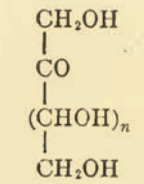
MONOSACCHARIDES

Simple sugars, or monosaccharides, containing 3, 4, 5, 6, and 7 carbon atoms occur in nature. They are called *trioses*, *tetroses*, *pentoses*, *hexoses*, and *heptoses*, respectively. Those of the aldose type which contain 5 and 6 carbon atoms (*aldopentoses* and *aldohexoses*) are most common.

Most of the monosaccharides may be represented by a formula of one of the following types:



Aldoses
($m = 1,2,3,4,$ or 5)

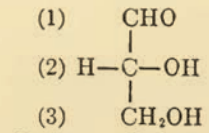


Ketoses
($n = 0,1,2,3,$ or 4)

Note that all the carbons are attached to each other and that each holds an oxygen. Carbon 1 of the aldoses and 2 of the ketoses are especially important because the most significant chemical reactions of the monosaccharides involve these points.

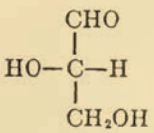
Stereoisomerism of monosaccharides

Organic molecules which contain an *asymmetric carbon, i.e.*, a carbon atom attached to four different atoms or groups, can exist in "right hand" or "left hand" forms. These are called *dextro* or D- and *levo* or L-forms, respectively. The simple sugars all contain carbon atoms of this asymmetric type, and hence can exist in the left- or right-handed patterns. For example, the triose, *glyceraldehyde*, has one asymmetric carbon (carbon 2, the center one):



Carbon number

D-Form



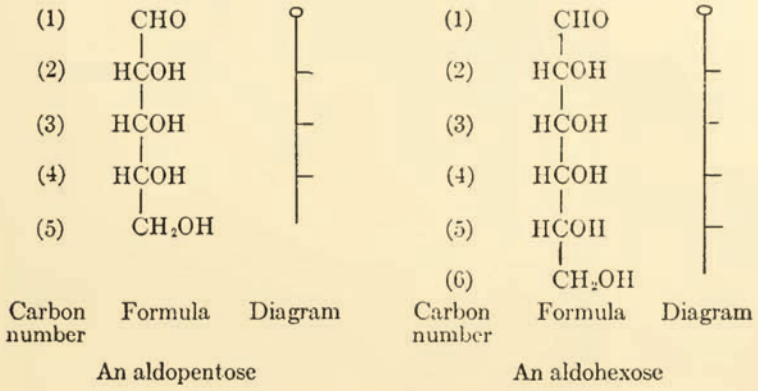
L-Form

Glyceraldehyde

The two forms in which this substance can exist are indicated by writing the —OH of carbon 2 on the right or on the left. When the aldehyde group is placed at the top of the formula, the D-form is the one with this —OH on the right. Such substances which differ from each other only in the way certain components of the molecule are arranged in space are called *stereoisomers*. The exact arrangement of one particular isomer is called its *configuration*.

When several asymmetric carbons are present in a molecule, D- and L-arrangements about each must be considered. The total number of stereoisomers in such cases equals $(2)^n$, where n is the number of different asymmetric carbon atoms. Therefore, there are 8 possible aldopentoses and 16 aldohexoses (see formulas below).

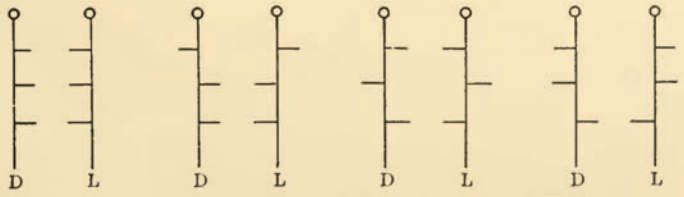
It is convenient to represent sugar isomers by means of diagrams which are related to the structural formulas of the sugars as shown:



An aldopentose — An aldohexose

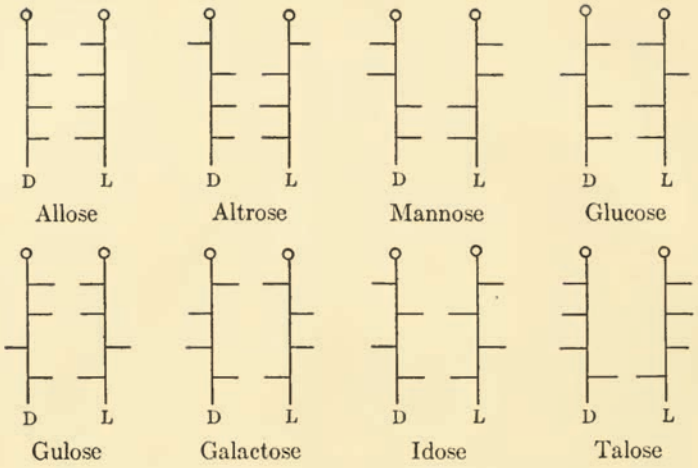
The small circle represents the aldehyde group (carbon 1), and the short side lines indicate which way the —OH on each asymmetric carbon extends from the chain. Aldopentoses have three asymmetric carbon atoms (2, 3, 4), while aldohexoses have four (2, 3, 4, 5).

The different aldopentoses and aldohexoses have the following formulas:



Ribose — Arabinose — Xylose — Lyxose

Configuration of stereoisomeric aldopentoses



Configuration of stereoisomeric aldohexoses

Note that the D-forms are those in which the configuration of the asymmetric carbon farthest from the aldehyde group, *i.e.*, carbon 4 in pentoses and 5 in hexoses, is the same as that in D-glyceraldehyde.

Optical rotation

Substances containing asymmetric carbons can also rotate polarized light.[1] If such light is passed through a solution of D-glyceraldehyde, for example, the emergent beam will be twisted a certain number of degrees. The amount of twisting is measured in an instrument called a *polarimeter*. This effect is called *optical rotation,* and substances which show it are said to be *optically active.* When measured under specified conditions, the angle of rotation is called the *specific rotation* and is a characteristic property of the optically active substance.

It is important to note that there is no necessary relationship between configuration and the sign of optical rotation. The D-forms may show either positive or negative rotation.[2]

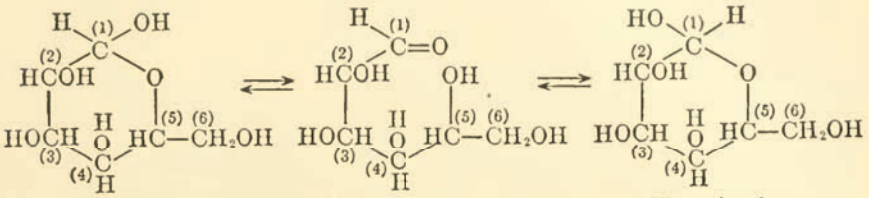
Cyclic formulas of monosaccharides

The aldose formulas have been written above in the "open-chain" or "free aldehyde" form. Certain properties of the aldoses indicate that an aldehyde group is present (combination with phenylhydrazine, for example, to form hydrazones or osazones). However, other properties

[1] This light vibrates in only one plane, as contrasted with ordinary light which vibrates in all possible planes. The student may visualize a polarized light beam as a flat, narrow ribbon of light.

[2] Positive rotation is clockwise rotation when you look toward the light source.

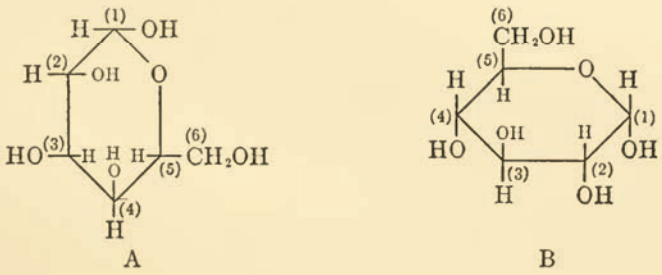
point to the absence of aldehyde groups (*e.g.*, failure to bind bisulfite or give the usual Schiff test [1]). The reason for this apparent contradiction is that most of the sugar at any one time exists in a cyclic or "oxide-ring" structure, which is derived by interaction of the aldehyde group with one of the —OH groups, usually at carbon 5:



Open-chain and ring formulas of D-glucose

Note that carbon 1 has now become asymmetric so that there are two stereoisomers of the ring structure. The alpha-forms of D-sugars have the —OH of carbon 1 on the *right* when the formulas are written as shown with carbon 1 on top. For sugars belonging to the L-series (see diagrams, pp. 23, 24) the alpha-ring forms have this OH on the *left*.

The oxide ring forms of the sugars are often represented diagrammatically. For example, for the above alpha-ring form:



Diagrams representing α-D-glucose

In *A* the diagram is drawn with carbon 1 at the top, but in *B* the molecule has been moved into a different position. The student should realize that the essential features of such formulas lie in the number and kind of atoms present, and in what order they are linked together. Whether the formulas are written with a particular part (*e.g.*, carbon 1 in the formulas above) at the top, side, or bottom, is incidental and merely a matter of convenience.

In the diagram *B* above, —OH groups shown pointing downward have

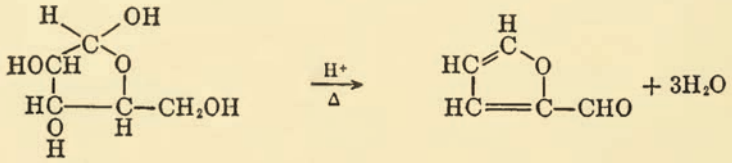
[1] Restoration of the pink color to Schiff's reagent, a dilute solution of rosaniline which has been decolorized with sulfurous acid.

the same configuration as those on the right in the open-chain formulas with carbon 1 on top.

The ring structures shown above are of the 1,5-oxide, or pyranose type, and are formed by aldohexoses, aldopentoses, and ketohexoses. Occasionally a 1,4-oxide or *furanose* ring is formed, as for example in the fructose component of sucrose (see p. 44).

Pentoses

There is no clear-cut evidence to show that pentoses occur *free* in plants. No free pentoses or characteristic derivatives of free pentoses have ever been isolated from seeds or green plants, or from any other natural source. Qualitative tests and quantitative data which were formerly attributed to free pentoses are now thought to be due to other compounds, such as glucuronic acid. A good test for pentoses depends on their conversion into furfuraldehyde by heating with fairly concentrated solutions of mineral acids:



An aldopentose (furanose ring form) — Furfuraldehyde

This product produces a brilliant rose-red color when warmed with aniline acetate, and therefore indicates the presence of pentoses. Hexuronic acids also give this test (p. 39) but hexoses do not, since they are converted by the acid treatment into levulinic acid, $CH_3COCH_2CH_2COOH$, which gives no color with aniline acetate.

Anhydrides of some of the pentoses are very abundant in plant materials, however, and therefore the corresponding pentoses can be easily prepared.

D-*Xylose.* Xylose is sometimes called wood sugar, as it can be made readily from wood, straw, seed hulls, and other fibrous materials. It is easily prepared from corn cobs by hydrolysis and crystallization. Corn cobs contain about 35 per cent of pentosans and yield about 12–15 g. of xylose per 100 g. of cob. The pure sugar sells for about $25 per pound, largely because there is not enough demand for it to make large-scale production worth while. It has been estimated that on a large scale it could be made for 5 cents per pound. Its use is limited almost entirely to bacteriological laboratories, where it is of considerable aid in the classification of bacteria.

L-*Arabinose.* This pentose is found in the form of complex polysaccharides in wheat and rye brans, in pectins, and in gummy materials

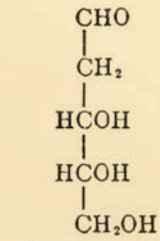
such as cherry gum, mesquite gum, and gum arabic. Such gums are frequently found associated with pectin in plant materials. Arabinose has also been obtained from peas and beans. In the laboratory it is generally made from sugar beet pulp or mesquite gum. The latter resembles gum arabic, being produced by a shrub which grows abundantly in Arizona and other states of the Southwest. Yields of arabinose amounting to 20 per cent can be readily obtained from the gum. Arabinose, like xylose, finds its chief use in bacteriological laboratories.

D-*Ribose.* Although from the standpoint of obtaining it in quantity, D-ribose is an exceedingly rare and expensive sugar (about $400 per pound); yet from the standpoint of its occurrence and functions in living organisms, it is one of the most common and important of the carbohydrates. It is present in all living cells as a component of ribosenucleic acids (see Chap. 6) and also as a part of several coenzymes (p. 273). Furthermore, two of the key substances involved in the process of muscle contraction, *adenosine diphosphate* (ADP) and *adenosine triphosphate* (ATP), are D-ribose derivatives.

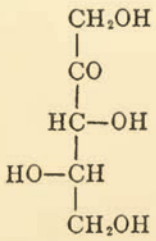
The pure sugar may be obtained by hydrolysis of yeast nucleic acid, or prepared synthetically from D-arabinose. The formula is indicated by the diagram on p. 23.

2-*Desoxy*-D-*ribose.* This sugar has been found only as a component of desoxyribonucleic acids, which are present in the nuclei of all living cells, specifically in the chromosomes of the nucleus (see Chap. 6). Therefore, it is of great interest as one of the chemical substances involved in the transmission of hereditary characteristics from one generation to the next.

As its name implies, the substance has the formula of an aldopentose, except that the oxygen on carbon 2 is missing, and has the configuration of D-ribose:



2-Desoxy-D-ribose



L-Xylulose

It is much more reactive and less stable than the ordinary aldoses or ketoses and is particularly distinguished by giving a positive aldehyde test with the Schiff reagent. This property of desoxyribose is the basis for the Feulgen and diphenylamine tests for desoxyribosenucleic acids.

L-*Xylulose.* This sugar, which has also been called L-xyloketose, is a ketopentose excreted in cases of human pentosuria.[1] From one to several grams may be excreted daily by a patient. L-Xylulose is so difficult to crystallize that it has been obtained only in the form of sirups. Crystalline derivatives are known, however, which serve to characterize and identify the sugar. It is an unusually strong reducing agent, as is shown by its ability to reduce Benedict's solution even at room temperature, whereas most other sugars give a positive result only upon heating.

Hexoses

D-*Glucose.* This sugar is also called dextrose. From the biological standpoint it is the most important carbohydrate in nature both because of its wide distribution and because of its prominence in physiological processes. It is the circulating carbohydrate of animals. Glucose is the sugar into which all the available carbohydrates of food are converted before oxidation in the body.

In the *free* state it occurs in practically all fruits, being especially abundant in grapes, figs, dates, and raisins. The blood contains about 0.08 per cent; in normal urine the amount may vary from traces to about 0.2 per cent. In diabetic urine the sugar sometimes rises to 10 per cent.

In the *combined* state it forms a part, or the whole composition, of many other sugars such as sucrose, lactose, and maltose. Starch, glycogen, and true cellulose yield glucose on complete hydrolysis. Certain substances known as glucosides yield on hydrolysis glucose together with some nonsugar compound often of characteristic odor or taste. An example of such a glucoside is amygdalin, the substance that gives the almond its peculiar flavor. Mustard owes its strong taste and odor to an oil produced from the glucoside, sinigrin. The following equation illustrates the action of the enzyme myrosin upon sinigrin:

$$\underset{\text{Sinigrin}}{C_{10}H_{16}NS_2KO_9} + H_2O = \underset{\text{Glucose}}{C_6H_{12}O_6} + \underset{\text{Mustard oil}}{C_3H_5NCS} + \underset{\text{Potassium acid sulfate}}{KHSO_4}$$

Formation of Glucose in Nature. The plant is the factory in which the world's food supply is manufactured. All animal life depends ultimately upon the vegetable world for its sustenance. Even carnivorous animals are indirectly supported by the plant; they prey on animals that feed upon plants. Man being an omnivorous creature receives a

[1] An abnormal condition characterized by the presence of a pentose sugar in the urine.

large part of his nourishment directly from plant sources. The synthesis of food from simple compounds is, therefore, a most fundamental operation, and it is the peculiar function of plants. The formation of glucose may be taken as typifying this synthesis, although recent investigations reveal that various sugar phosphates and sucrose are formed before glucose (see p. 397).

Carbon dioxide from the air and water from the soil are converted in the leaves of plants into the various carbohydrates. Since sunlight furnishes the energy required for the synthesis of carbohydrates, this process is known as *photosynthesis*. The net result of the process is often represented by the following equation:

$$6CO_2 + 6H_2O + 717.6\ \text{Cal.} = C_6H_{12}O_6 + 6O_2$$

In this equation $C_6H_{12}O_6$ stands for a hexose sugar such as glucose. Additional details are given in Chap. 15.

The most important point to note in connection with photosynthesis is that energy, 717.6 Cal. for a gram molecule of hexose sugar (180 g.), is required to cause the reaction to take place. The energy thus stored becomes available to man and other animals when the carbohydrate is oxidized in the body:

Oxidation or respiration

$$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O + 683\ \text{Cal.}^1$$

The supply of carbon dioxide furnished by animals and microorganisms enables the plant to continue its life processes. Plants, animals, and microorganisms are so interdependent that no one class could function in its normal manner without the activities of the other two.

Preparation of Glucose. Commercial glucose is made from starch, corn starch in the United States and potato starch in Europe. To prepare a glucose sirup the starch is suspended in water containing a small amount of hydrochloric acid (0.6 per cent) and is heated under pressure until the solution fails to give a red color with iodine, at which point the solution still contains a large proportion of partially hydrolyzed carbohydrate. The acid is neutralized, and the liquid is decolorized with powdered adsorptive charcoal and concentrated to a thick sirup containing about 80 per cent solids. Large quantities of this *flat* sirup are used in making candy. For table use, cane sirup is added to the flat sirup to give it a better flavor; this is the so-called "corn" sirup. Owing to certain peculiarities that it possesses, glucose is, in certain respects,

[1] The apparent discrepancy between 717.6 and 683 Cal. is due to differences in the concentration and state of the reactants and products in the two processes (see pp. 395 and 414).

superior to sucrose for the making of fondants, creams, fancy candies, chewing gum, doughnuts, and other products.

To prepare crystalline glucose the hydrolysis is carried to completion; the sugar solution is then concentrated in an evaporator to a density of 1.36 to 1.45. The concentrated sugar solution is then introduced into crystallizing vessels that contain some of the crystals from the preceding batch. This practice of seeding the liquor is an essential step in obtaining crystals of approximately the desired size and uniformity. The crystals of hydrated glucose are separated from the mother liquor by means of centrifugal machines, washed in the same machines, and then sent through a drier. In 100-pound bags it now sells for about 8 cents per pound.

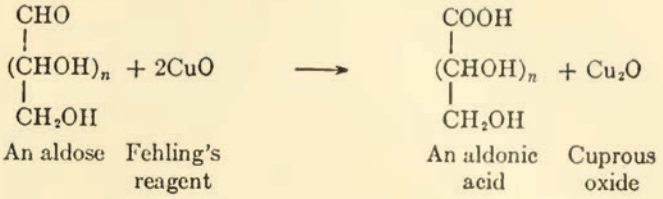
The *sweetness* of glucose is approximately 75 per cent of that possessed by our common sugar, sucrose. Its *calorific value,* however, is about equal to that of sucrose. Glucose is readily *fermented* by practically all microorganisms. The spoilage of fruits and vegetables is accompanied by a destruction of glucose. The manufacture of alcoholic beverages is based upon the fermentation of glucose by yeast.

The most characteristic chemical property of glucose is its reduction of solutions of copper salts with the formation of a precipitate, cuprous oxide. The color of the precipitate varies from yellow to brick red, depending upon the fineness of the particles of oxide. Some of the most common copper reagents used in sugar tests are Fehling's (copper sulfate, sodium potassium tartrate, and sodium hydroxide), Benedict's (copper sulfate, sodium citrate, and sodium carbonate), and Barfoed's (copper acetate and acetic acid) solutions.

Glucose reduces these reagents because it is oxidized by the cupric ion (Cu^{++}) present. The process is dependent on the presence of the aldehyde group in the glucose molecule or, in general, on the presence in the sugar tested of an aldehyde or ketone group not attached to other atoms in the form of a glycoside (p. 40). However, it is immaterial whether the sugar is in the open chain or oxide ring form. In the latter, the aldehyde (or ketone) group is apparently covered up, but it is still a *potential* aldehyde group because of the easy interconversion of the chain and ring forms in solution.

Many other aldehydes such as formaldehyde, acetaldehyde, and chloral also have reducing power. Reduction of Fehling's solution and similar reagents must, therefore, be recognized, not as the peculiar attribute of sugars, but rather as a general property common to many substances.

The chemical changes which reducing sugars undergo during the Fehling's test are very complex. Certainly one main reaction is oxidation of the aldehyde group to a carboxyl with the formation of the corresponding aldonic acid:



The copper of Fehling's solution is actually present as a copper compound of sodium potassium tartrate, $NaKCuC_4H_2O_6$, but CuO more clearly indicates the oxidizing character of the solution.

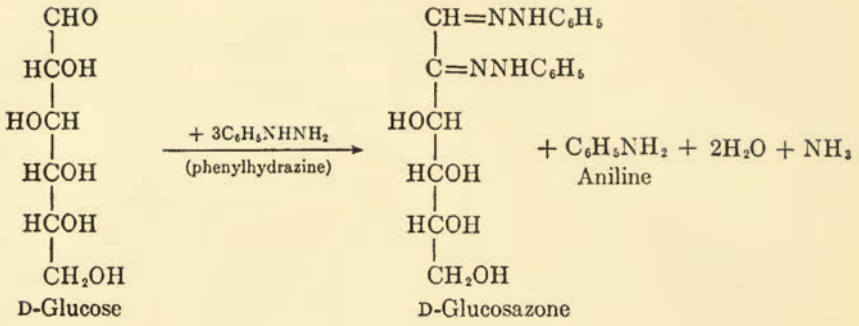
The above reaction accounts for less than half of the cuprous oxide actually produced during the Fehling's reaction. The rest is produced indirectly by the oxidation of simpler substances into which the reducing sugars are converted by the strong alkali (sodium hydroxide) in the reagent. Decomposition by alkali is a characteristic property of reducing sugars generally. Nef isolated 93 substances from the decomposition of sugars in alkaline solution.

Benedict's solution is a less sensitive reagent for reducing sugars than Fehling's solution because it contains a weaker alkali, sodium carbonate. This is an advantage, since it is used to test for sugar in urine, which commonly contains small amounts of nonsugar reducing substances. These materials are less apt to give a false result with Benedict's than with Fehling's solution. Barfoed's reagent is not alkaline at all, but rather is acidic; hence it requires a very strong reducing agent to produce a positive result. It is for this reason that the Barfoed's reagent can be used to distinguish simple sugars from other carbohydrates (see p. 42).

Any sugar capable of reducing Fehling's solution is called a *reducing sugar*. All monosaccharides are reducing sugars, as are also the common disaccharides, maltose, lactose, and cellobiose (but not sucrose). Fehling's reaction forms the basis of a useful method of analyzing foods for their sugar content. A weighed sample is extracted with hot water, and a portion of the solution so obtained, after treatment to remove interfering substances, is hydrolyzed and allowed to react with Fehling's solution under carefully standardized conditions. The precipitate of cuprous oxide is collected and weighed, and from the weight found the percentage of sugar in the sample may be calculated.

In the analysis of fruits, vegetables, sirups, candies, blood, urine, and so on, total reducing sugar is generally expressed as glucose. No attempt is made to distinguish between glucose or fructose as both have the same nutritive value and approximately the same reducing power.

Glucose reacts with an excess of phenylhydrazine to form an insoluble precipitate known as *glucosazone* according to the following equation:



This precipitate is made up of long yellow needles, usually arranged in a broom-like or sheaf structure. The osazone is frequently of great help in establishing the presence of glucose in a digestion product, fruit juice, or other saccharine substance. It cannot be relied upon alone, however, because all reducing sugars give osazones. In fact, D-fructose and D-mannose produce the same osazone as D-glucose does. In many cases, however, the crystalline form, and more particularly the optical rotation and melting point of the osazones, are of great help in identifying individual sugars.

D-*Galactose*

Galactose does not occur free in nature but is found combined with other sugars in many carbohydrates and related compounds. Each of the sugars, lactose and raffinose, gives one molecule of galactose on hydrolysis, and certain polysaccharides, the galactans, yield galactose as the chief hydrolytic product. Legumes, impure pectin, agar, and Douglas fir and other coniferous woods are other galactose-yielding materials. Galactose is also a constituent of certain galactosides found in brain and nerve tissue, and of many animal proteins. Its occurrence in these physiologically important tissues gives to galactose added significance and importance.

Galactose is generally made from lactose by hydrolysis and crystallization. Aside from the small amount required by bacteriological laboratories for the study of the fermentation characteristics of bacteria, there is no particular demand for it.

Most bread yeasts do not ferment galactose, but many wild yeasts ferment it readily. Bacteria, generally speaking, attack it more slowly than either glucose or fructose. Being an aldose, galactose reduces Fehling's solution and gives a characteristic osazone with phenylhydrazine.

The most distinctive property of galactose is the formation, when

oxidized with nitric acid, of an insoluble dibasic acid, mucic acid. The formation of mucic acid is used both as a qualitative and quantitative test for the presence of galactose-yielding compounds. It is of use in showing that milk has been used in the preparation of milk chocolate, infant foods, and other preparations. The following equation indicates the nature of the reaction:

$$\underset{\text{Galactose}}{CH_2OH(CHOH)_4CHO} + 3O = \underset{\text{Mucic acid}}{COOH(CHOH)_4COOH} + H_2O$$

The occurrence of L-galactose among the hydrolysis products of flaxseed mucilage has been reported recently. Galactose is one of few sugars (arabinose is another) which, thus far, has been found to occur in nature in both D- and L-forms.

D-*Mannose*

Mannose does not occur in the free state in nature. However, it is widely distributed in *mannans,* polysaccharides that yield mannose on hydrolysis—compare fructosan, galactan, pentosan. That mannose may play an important role in animal physiology is indicated by relatively recent observations. Mannose is a constituent of egg albumin (1.77 per cent), serum albumin (0.45 per cent), and many other proteins (0.3–4.0 per cent).

The hexahydric alcohol mannitol, $C_6H_8(OH)_6$, corresponding to mannose, is also widely distributed in nature. It has been found in the pineapple, onion, green bean, cauliflower, olive, mushroom, and in the bark and leaves of many trees. It is the chief constituent of Sicilian manna, a sweet exudate produced by a certain species of ash when incisions are made in the bark. Many other trees and shrubs produce mannas of varying composition as a result of the sting of certain insects. It is supposed that the manna upon which the Israelites subsisted during their wanderings in the wilderness was an exudate secreted by a species of tamarisk tree. In Australia, India, and other countries manna from different species of trees is used as a food by the natives. Many different kinds of sugar have been isolated from these mannas.

D-*Fructose*

Fructose, also called levulose, is widely distributed in nature, and in the *free state* is generally associated with glucose and sucrose. It is particularly abundant in fruit juices, whence comes the name fruit sugar. Vegetables, the nectar of flowers, and the sap of green leaves and stalks also contain fructose and glucose. Honey contains about equal quantities

(40 per cent each) of these two sugars. The two occur frequently in nearly equal amounts, and since they both are formed by hydrolysis of sucrose, it is supposed that the two originate from the action of the enzyme sucrase on sucrose. In some fruits such as apples and pears, fructose seems to be more abundant than glucose, however.

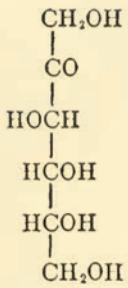
Raffinose and melezitose are two other sugars that yield a molecule of fructose on hydrolysis. The polysaccharide inulin gives only fructose on hydrolysis and thus stands in the same relation to fructose as starch does to glucose. Fructose may be prepared from either sucrose or inulin, but more easily from the latter.

In recent years considerable effort has been expended in an attempt to produce fructose, or levulose as it is called in trade, on a commercial scale. There would be a great demand for levulose at a reasonable price because of its marked sweetening power—nearly twice that of sucrose. The most promising source is the Jerusalem artichoke, a plant which grows well in temperate climates and yields a high tonnage of tubers per acre. The tubers are sliced and the sugars extracted in much the same way as sucrose is extracted from the sugar beet. After hydrolysis of the juice, levulose is precipitated as the calcium compound. This is removed, decomposed by carbon dioxide, and the free sugar is obtained either in the form of a sirup or, by careful concentration and cooling of the sirup, as the crystallized product.

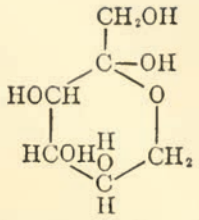
Neither glucose nor fructose crystallizes readily, but fructose has a particularly strong tendency to remain in a sirupy condition. This is well illustrated by honey, in which the glucose generally crystallizes after two or three months storage, while the fructose remains in a sirupy state. Browne states that "the granulation of honey was known to the ancients and crystallized glucose as thus observed was probably the first sugar known to mankind."

If fructose and glucose are present in the sirup from cane or sugar beet, they interfere with the crystallization of the sucrose. This property is used to advantage in the preparation of cane sirup from sucrose. Sucrase, an enzyme obtained from yeast, is added to the warm sirup and allowed to hydrolyze the sucrose for about 12 hours. At the end of this time the sirup is further concentrated and may be stored without danger of crystallizing. A similar effect is produced by the partial hydrolysis of sucrose in making jelly and fondant. If sufficient fructose and glucose are present, the unhydrolyzed sucrose is prevented from crystallizing and a smooth even texture results. Whenever sucrose crystallizes, it imparts a rough gritty texture to the candy or jelly.

D-Fructose is a ketohexose with the same configuration as D-glucose about carbon atoms 3, 4, and 5:



Open-chain formula

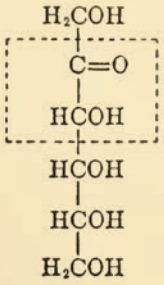


Pyranose ring formula

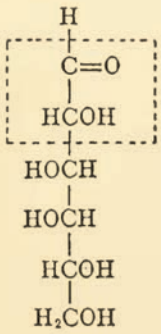
D-Fructose

Many of the properties of glucose that have been noted are possessed by fructose also. It is readily fermented by yeast and bacteria. By the action of certain mannitol-forming bacteria (for example, *L. pentoaceticus*) fructose is reduced to the hexahydric alcohol, mannitol. This change takes place in the making of sauerkraut, silage, and certain wines.

Fructose and other ketoses reduce Fehling's solution and give the other tests associated with reducing power fully as well as do aldoses. The structure responsible for this reducing power is the ketone group situated next to an alcohol group, thus: $\begin{matrix} C=O \\ | \\ HCOH \end{matrix}$. In fact, this same structure is present in aldoses, as is illustrated below:



Ketohexose



Aldohexose

As in the case of glucose, the sodium hydroxide in Fehling's solution also brings about the decomposition of fructose into many simpler substances, which become oxidized and contribute to the formation of the cuprous oxide precipitate.

With phenylhydrazine, D-fructose forms an osazone, which is identical with D-glucosazone and D-mannosazone (note identical structure and configuration of carbons 3 to 6 in the formulas of these three sugars).

The optical rotation of D-fructose, however, is very different from that of D-glucose, being −92.4° as compared to +52.7° (see Table 3–2).

Fructose and other ketoses can be distinguished from aldoses by the resorcinol test, which consists in the production of a blood-red color when a ketose is boiled with a solution of resorcinol in hydrochloric acid. Since other ketoses are not common, a positive resorcinol test is a good indication of the presence of D-fructose or of other carbohydrates which produce D-fructose on hydrolysis (sucrose, raffinose, melezitose, inulin, etc.).

Table 3–2

Melting points and optical rotations of common sugars

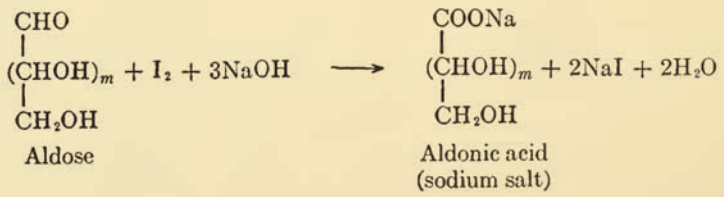
Sugar	*Melting point* [°C]*	*Optical rotation* $[\alpha]_D$†	*Sugar*	*Melting point* [°C]	*Optical rotation* $[\alpha]_D$
D-Xylose	145	+18.8	L-Sorbose	161	−43.4
D-Arabinose	160	−104.5	D-Glucosamine	110	+70 ††
L-Arabinose	160	+104.5	D-Glucuronic acid	156	+36.3
D-Ribose	87	−23.7	Lactose	202	+52.6
D-Glucose	146	+52.7	Sucrose	188	+66.5
D-Galactose	167	+80.2	Maltose	103	+130.4
D-Mannose	163	+14.2	Cellobiose	225	+34.6
D-Fructose	104	−92.4	Trehalose	97	+178.3

* Of form obtained most commonly.

† Specific rotation of the equilibrium mixture of α and β forms (if any) measured in water at or near 20°C.

†† Hydrochloride.

Ketoses are also differentiated from aldoses by greater resistance to mild oxidative treatments. For example, under proper experimental conditions aldoses can be converted almost quantitatively into the corresponding *aldonic acids* by oxidation with iodine in alkaline solution according to the equation:

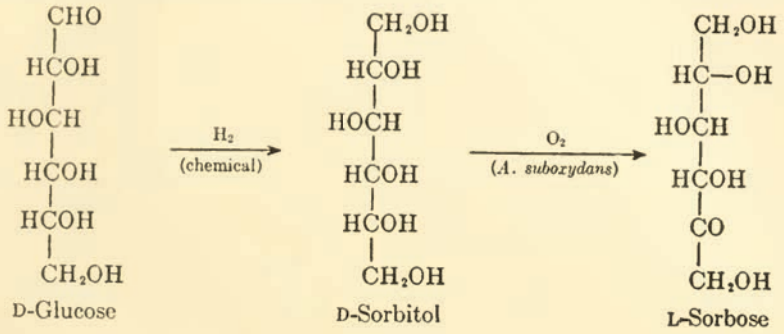


Under identical conditions ketoses remain practically unaffected.

L-*Sorbose*

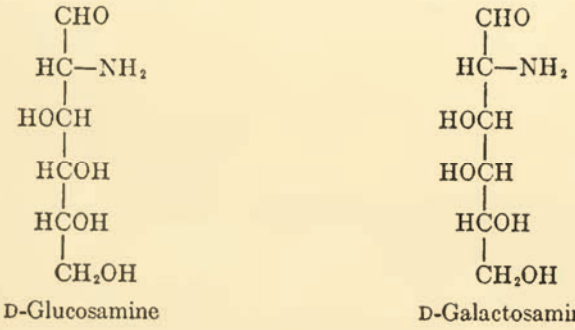
This ketohexose is found in nature only in the fermented juice of mountain ash berries, where it undoubtedly arises as a result of bacterial oxidation of D-sorbitol. As an industrial product, however, it has acquired

considerable importance in recent years because it is an intermediate in the synthesis of vitamin C. It is produced on a commercial scale by selective bacterial oxidation of D-sorbitol with *Acetobacter suboxydans*. The necessary sorbitol is produced by the chemical reduction of D-glucose:



Hexosamines

The two amino sugars found in nature are related to common aldohexoses and in each instance bear the amino group on carbon 2:

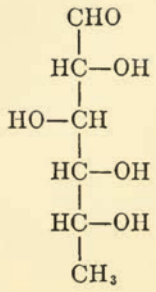


D-Glucosamine (chitosamine) is the sole constituent sugar formed by hydrolysis of chitin; it is also a component of mucin and several other animal and bacterial polysaccharides. An unusual derivative, N-methyl-L-glucosamine, is one of the components of *streptomycin*, an important antibiotic. The chief natural occurrence of D-galactosamine (chondrosamine) is as a component of chondroitin in cartilage (p. 67).

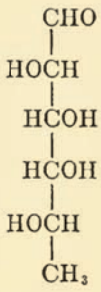
Both sugars show the reactions of aldohexoses (reducing power, osazone formation) and, in addition, have the basic properties of the amino group.

Desoxyhexoses

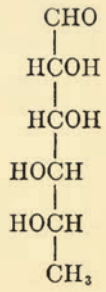
These sugars, which are also known as methyl pentoses, lack the oxygen atom on carbon 6:



6-Desoxy-D-glucose



6-Desoxy-L-galactose
(L-fucose)

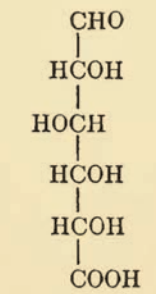


6-Desoxy-L-mannose
(L-rhamnose)

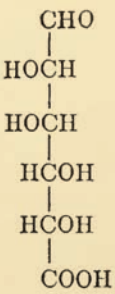
They are found in many plant species, particularly in the form of glycosides. These substances show the usual properties of monosaccharides, except that on heating with strong acids they yield 5-methyl furfural (contrast aldopentoses, aldohexoses). L-Rhamnose is probably the most abundant of these three sugars in nature. It is one of the component sugars in several plant gums and mucilages (p. 66), in the important heart stimulant drugs known as cardiac glycosides, and is present in at least two antibiotics of bacterial origin. These particular antibiotics represent an interesting chemical type because they consist of the sugar, L-rhamnose, attached to a fatty acid, beta hydroxy decanoic acid.

Uronic acids

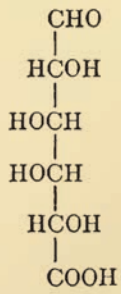
Those simple sugar derivatives which have both an aldehyde and a carboxyl group are termed *uronic acids*. Three occur in nature, all related to aldohexoses:



D-Glucuronic acid



D-Mannuronic acid



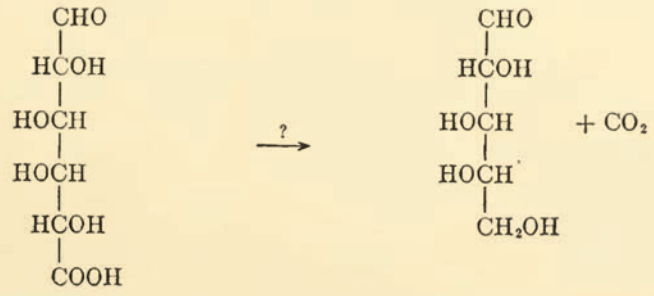
D-Galacturonic acid

D-Glucuronic acid is found in the animal body as a component of mucopolysaccharides (p. 67) such as heparin and chondroitin. It is utilized by the body to detoxify various harmful drugs which may be ingested. For example, if dogs are fed borneol, it is excreted in the

urine as borneol glucuronide. A number of bacterial carbohydrates, particularly the immunopolysaccharides, form D-glucuronic acid on hydrolysis. It is also a component of nearly all of the plant gums such as gum arabic and cherry gum.

D-Galacturonic acid is perhaps best known as the fundamental building block of pectic acid, although it is also one of the components of many plant mucilages. When hydrolyzed, alginic acid, from sea weeds, yields D-mannuronic acid as the only primary product.

The most characteristic chemical property of the hexuronic acids is the ease with which they lose carbon dioxide (decarboxylation) on heating with mineral acids. The carbon dioxide production is essentially quantitative, being used both for detecting uronic acids and for determining their quantity. It is possible that pentoses arise in nature from hexuronic acids, since members of each group with corresponding configurations often occur together, *e.g.*, D-galacturonic acid and L-arabinose:



D-Galacturonic acid L-Arabinose

However, pentoses cannot be isolated from the products of the chemical decarboxylation of the uronic acids. Furfural is formed as from pentoses, but in smaller yields up to about 40 per cent, whereas pentoses give 70–80 per cent of the theoretically possible amount.

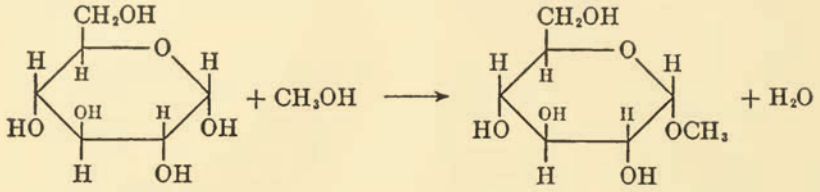
A qualitative test for hexuronic acids consists in boiling with hydrochloric acid and naphthoresorcinol. A blue pigment is formed which can be extracted with the organic solvents, ether or benzene. Pentoses and a few other sugars give a similar test. In fact pentoses and uronic acids in general tend to show similar properties, except for the carbon dioxide evolution already mentioned.

DISACCHARIDES

Glycosides

Simple sugars have a marked ability to combine with other molecules which contain —OH groups. The combination always involves the —OH group on carbon 1 of the simple sugar if it is an aldose, or 2 if a ketose,

both being in the oxide ring form. The process may be illustrated by the combination of glucose with methyl alcohol:

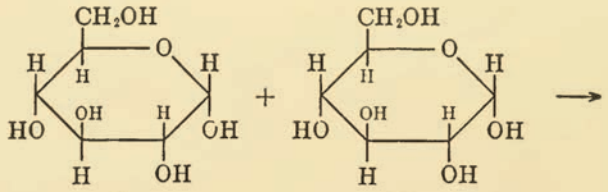


α-D-Glucose — Methyl α-D-Glucoside

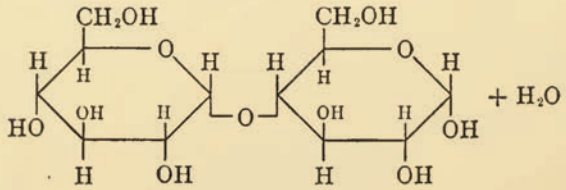
As a class such substances are termed *glycosides*, but individual members are named from the component parts, as indicated in the above example. Both α- and β-glycosides may be formed from the corresponding α- and β-sugars.

The glycosides do not show the simple sugars' characteristic properties of reducing power or osazone formation because the aldehyde or ketone group is covered up. Glycosides are rather stable to alkalies but are hydrolyzed by acids to form the original components.

If the second molecule with which a monosaccharide combines happens to be that of another monosaccharide, the product is a *disaccharide*. A disaccharide may therefore be defined as a glycoside formed from two simple sugar molecules by removing one molecule of water.[1] The second simple sugar may be either the same kind or a different kind from the first. For example, two molecules of glucose may combine as follows:



α-D-Glucose — α-D-Glucose



4-D-Glucosyl-α-D-glucose

The product in this case is an α-D-glucoside with the second glucose unit attached through its carbon 4; it is therefore called 4-D-glucosyl-α-

[1] This statement is intended to be a definition only. Disaccharides probably are not actually produced in living cells by removing water from simple sugars (see p. 399).

D-glucose. This particular disaccharide is *maltose*. The "disaccharide linkage" connecting the two simple sugar units in this case is an α-type and goes from carbon 1 of one unit to 4 of the other. This is often abbreviated to an "α-1,4-linkage."

Any alteration in the nature of the disaccharide linkage, or in the component sugars, results in a different disaccharide. For example, two glucose units combined by a β-1,4 linkage form the disaccharide, *cellobiose*, which is a substance distinctly different from maltose. The chemical make-up of the more common disaccharides is shown in Table 3–3.

Table 3–3

Chemical constitution of disaccharides

Common name and component sugars	*Disaccharide linkage*	*Chemical name**
Sucrose:		
D-glucose	α, β-1, 2	1-α-D-glucosyl-β-D-fructose
D-fructose		
Lactose:		
D-glucose	β-1, 4	4-D-glucosyl-β-D-galactose
D-galactose		
Melibiose:		
D-glucose	α-1, 6	6-D-glucosyl-α-D-galactose
D-galactose		
Maltose:		
D-glucose	α-1, 4	4-D-glucosyl-α-D-glucose
D-glucose		
iso-Maltose:		
D-glucose	α-1, 6	6-D-glucosyl-α-D-glucose
D-glucose		
Cellobiose:		
D-glucose	β-1, 4	4-D-glucosyl-β-D-glucose
D-glucose		
Gentiobiose:		
D-glucose	β-1, 6	6-D-glucosyl-β-D-glucose
D-glucose		
Trehalose:		
D-glucose	α, α-1, 1	1-α-D-glucosyl-α-D-glucose
D-glucose		

* For simplicity, the designation of furanose and pyranose rings has been omitted from these names. All are pyranose except for the fructose unit in sucrose (see structural formulas for the individual disaccharides).

The disaccharides may or may not have reducing properties, depending on whether the disaccharide linkage involves the aldehyde (or ketone) group of only one of the component simple sugars, or of both. In the latter case since no free, or potentially free, aldehyde or ketone group remains in the disaccharide, it therefore gives no osazone and does not respond to the Fehling's or other similar tests. The structures of sucrose and trehalose are of this nonreducing type.

On the other hand such disaccharides as maltose, lactose, and the others in Table 3–3 do contain a potential aldehyde group and show the characteristic reactions of reducing sugars, although to a smaller degree than the monosaccharides. This lowered reducing power is not surprising when it is remembered that even in the reducing disaccharides one reducing group has been covered up in forming the disaccharide linkage. The Barfoed test for monosaccharides is based on the stronger reducing power of the simple sugars as compared to the disaccharides.

Like other glycosides, the disaccharides can be hydrolyzed, whereupon they take on a molecule of water and form the corresponding simple sugars. This hydrolysis may be brought about by heating the disaccharide with dilute acid, or by the action of certain enzymes. Such hydrolytic enzymes are found in the digestive tracts of animals, in yeasts, bacteria, and molds, and in many higher plants. The enzymes are named according to the sugar upon which they act; sucrase (also called invertase) acting on sucrose, maltase on maltose and lactase on lactose. The equation of hydrolysis is as follows:

$$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6$$

Sucrose	Glucose	Fructose
Maltose	Glucose	Glucose
Lactose	Glucose	Galactose

The mixture of glucose and fructose formed by hydrolysis of sucrose is called "invert sugar." Obviously it consists of equal parts of glucose and fructose.

Sucrose

This sugar is known also as saccharose, cane sugar, beet sugar, or simply "sugar." As already stated in connection with glucose and fructose, sucrose is generally associated with these monosaccharides in flowers, fruits, roots, and seeds of plants. It is especially abundant in sugar *cane*, sugar *beet*, sorghum, and the sap of the maple and palm. The first two plants, which contain 16–20 per cent sucrose, are the chief commercial sources of this sugar. Sorghum contains an abundance of sucrose, but it has not as yet been possible to produce sugar successfully from this plant.

Annual world production of raw sugar during the last 5 years has been 30–35 million tons, and is still rising. About two-thirds of the total is produced from sugar cane and nearly all of the rest from sugar beets. The United States and its island possessions, together with the Philippine Islands, produce about one-sixth of the world total. Louisiana and Florida are the leading cane sugar states; California and Colorado, the beet sugar states.

The annual per capita consumption of sugar in the United States is

very high, running to over 100 lbs. in most years. The desirability of such a large consumption of sugar is doubtful. Sugar supplies about one-sixth of the caloric intake and hence displaces the consumption of less-refined foods that would carry minerals and vitamins as well as energy. Sherman, who has given much thought to this matter, suggests that, instead of devoting so much land, labor, and money to the production of sugar, it would be a wiser policy to increase the production and consumption of foods which furnish needed nutrients as well as calories. However, it should be pointed out that sucrose is one of the very cheapest sources of food energy. A comparison of various low-cost foods from this standpoint is given in Table 3–4.

The manufacture of sucrose is an excellent example of a chemically controlled industry. From the determination of the sugar content of the raw beet to the analysis of the finished product, it is an application of the principles involved in the preparation of any pure chemical. Extraction, clarification, evaporation, and crystallization are the important steps involved. Because of the ease with which sucrose crystallizes, it lends itself readily to this method of purification.

Sucrose is sweeter than glucose but not so sweet as fructose. It is claimed by the majority of investigators that invert sugar, which is formed when sucrose is hydrolyzed, is sweeter than sucrose, but there is considerable difference of opinion on this point. It is difficult to determine the comparative sweetening power of sugars owing to the fact that small differences in concentration cannot be detected by the sense of taste. For example, sucrose solutions differing by less than 1.5 per cent cannot be readily distinguished. Some of the sugars have other tastes than that of sweetness, which complicates the comparison. The comparative sweetness of sugars, giving sucrose a value of 100, has been rated as follows: lactose 16, raffinose 23, galactose 32, rhamnose 33, maltose 33, xylose 40, glucose 74, sucrose 100, invert sugar 130, fructose 173.

In cooking operations, such as the making of jelly where sucrose is hydrolyzed, it would seem that the proper time to add the sucrose is at the beginning of the cooking. This insures the maximum hydrolysis of sucrose, and consequent maximum sweetening power. Moreover, the hydrolysis products, glucose and fructose, prevent crystallization (graining) of unhydrolyzed sucrose and give the best conditions for producing a jelly of smooth texture. Approximately 50 per cent of the added sucrose is converted into invert sugar by the usual methods of jelly making. Any cooking operation that involves the use of sucrose and acid, such as the canning of fruit and making of jams and of many kinds of pie, will bring about a considerable hydrolysis of sucrose. It is probable that in many other cooking operations sucrose undergoes slight hydrolysis as a result of the effect of salts and other food constituents.

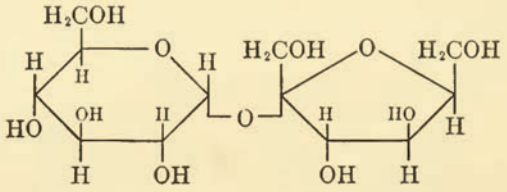
Table 3–4

Cost of food calories as provided by various low-cost foods

Food	*Price per pound* [cents] *	*Calories per pound*	*Cost per 100 calories* [cents]
Potatoes	5	377	1.32
Bread, white	14	1250	1.12
Macaroni	17	1710	1.00
Rice	15	1670	0.90
Beans, dry	13	1530	0.85
Flour, patent	9	1650	0.55
Sucrose	10	1750	0.57

* Retail prices at Madison, Wisconsin, January, 1952.

The chemical constitution of sucrose is expressed by the following formula:



α-Glucoside part β-Fructoside part

Sucrose

Note that the disaccharide linkage is α,β-1,2 and involves the original reducing groups of each of the component simple sugars. Hence sucrose does not reduce Fehling's solution or give an osazone with phenylhydrazine. It is fermented by yeast and by most bacteria. Strictly speaking, sucrose is not fermented because it is first hydrolyzed; the resulting glucose and fructose undergo the fermentation. Likewise, in the utilization of sucrose by the body, hydrolysis precedes absorption.

Sucrose may be estimated either by chemical means or through the aid of a saccharimeter.[1] (See optical rotation.) If reducing sugar is determined *before* and *after* hydrolysis, the increase in reducing sugar furnishes a means of calculating sucrose. Since a molecule of water is added during the hydrolysis, 95 per cent of the invert sugar (increase in reducing sugar) is equivalent to the sucrose in the sample. For example:

	per cent
Reducing sugar before hydrolysis	4.36
Reducing sugar after hydrolysis	9.28
Invert sugar	4.92
Sucrose, $.95 \times 4.92$	4.67

[1] This is a polarimeter especially calibrated to read percentage of sucrose in the solution tested rather than the angle of rotation of the polarized light.

The figure 95 per cent is obtained from the hydrolysis equation of sucrose and is the ratio of the molecular weight of sucrose to the sum of the molecular weights of glucose and fructose, the sugars of which invert sugar is composed ($342 \div 360 = 0.95$).

Optical Rotation of Sucrose. The rotation of polarized light is the basis for determining sucrose by means of a saccharimeter. This instrument enables the beet sugar manufacturer to determine what he should pay for his beets and the custom house official to decide what should be the import duty on a cargo of sugar. It is as important to the sugar industry as the "Babcock Tester" is to the dairy industry and serves as an outstanding example of an abstract physical property becoming of great economic value.

Sucrose is dextrorotatory (+66.5), but invert sugar is levorotatory (−19.85) because fructose rotates polarized light more to the left (−92.4) than glucose does to the right (+52.7). Because the rotation is reversed (inverted) when sucrose is hydrolyzed, the hydrolysis of sucrose is called "inversion." The change in the direction of rotation is also the reason for the terms "invert sugar" and "invertase"—the name of the enzyme that effects the hydrolysis. Sucrase is a better name for this enzyme because it denotes which sugar is hydrolyzed. The term "inversion" can be properly applied only to the hydrolysis of sucrose because the hydrolysis of other sugars is not accompanied by a change in the direction of optical rotation. By determining the *rotation* of a sugar solution, for example, from cane, beets, fruits, and so on, *before and after* hydrolysis, the *percentage of sucrose* may be determined because the *change in rotation* is directly proportional to the *quantity of sucrose* present. The saccharimeter enables the analyst to determine in a few minutes the percentage of sucrose and thus puts all operations in the sugar industry on an exact basis.

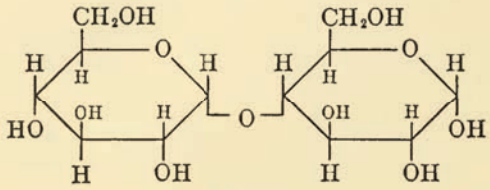
Maltose

This disaccharide is widely distributed in leaves and young seedlings and is especially abundant in germinating seeds. It is the principal sugar formed by the action of the digestive enzymes ptyalin and amylopsin on starch and glycogen. In the germination of seeds a starch-splitting enzyme, diastase, is produced and brings about the conversion of the insoluble starch into a soluble sugar, maltose, which is utilizable by the plant cells. Additional information on starch-splitting enzymes is given on p. 58.

Malt sirups can be made from the water-soluble material of germinated barley. Also a sirup can be prepared from the sweet potato by steeping the finely cut potato in water at 40°C. for a few hours. After being filtered from insoluble material, the solution is concentrated to a thick sirup, having the flavor of the sweet potato.

Malted milks and certain infant foods contain the water-soluble material of germinated barley. The water extract, evaporated to dryness and mixed with the other ingredients, imparts the peculiar malt flavor to these products. Pure maltose can be prepared by digestion of starch with diastase, followed by evaporation and crystallization from 60 per cent alcohol. It is not much used in the crystalline form.

As is indicated by its formula, maltose is a reducing type disaccharide:



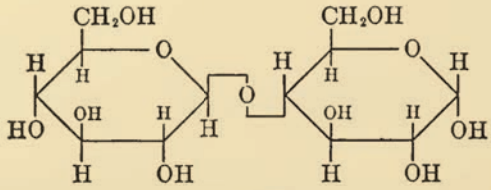
Maltose

Note that carbon 1 of the right-hand glucose unit, as the formula is written above, is an aldehyde group in the oxide-ring form (compare with the formula of α-D-glucose, p. 25). It therefore gives a positive test with Fehling's solution and an osazone with phenylhydrazine. The osazone is rather soluble in water but usually separates on cooling in the form of daisy-like crystals (Fig. 3–1). Note also that the two glucose units are held together in an α-1,4-linkage. This same type of linkage is present in several of the more common polysaccharides such as starch and glycogen.

Yeasts, bacteria, and other microorganisms ferment maltose with about the same ease that they ferment glucose. It is assumed that the maltose is first hydrolyzed and then fermented.

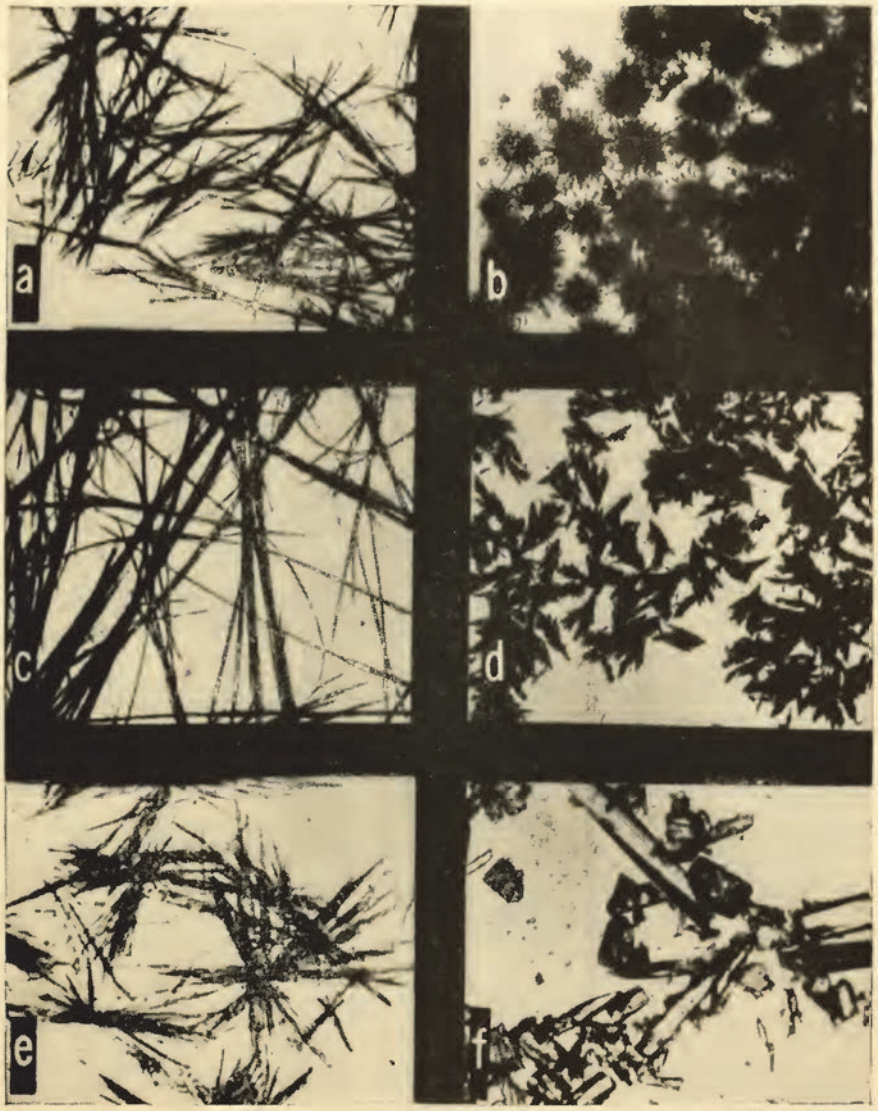
Cellobiose

Like maltose, this disaccharide, which does not occur free in nature, is composed of two glucose units attached through the 1 and 4 positions, but unlike maltose, the disaccharide linkage is the β-type:



Cellobiose

Note that in the left-hand glucose unit, as the formula is written above, the configuration of carbon 1 is β, whereas in maltose it is α. This is the only structural difference between cellobiose and maltose. Cello-



Courtesy of W. F. Hassid.

Fig. 3–1. Crystalline form of derivatives of various sugars: (a) glucosazone, (b) lactosazone, (c) xylosazone, (d) maltosazone, (e) galactosazone, (f) mucic acid.

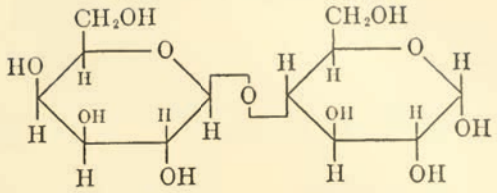
biose is of interest particularly in connection with the chemistry of cellulose, which also is built up from glucose units attached to each other through β-1,4-linkages. Cellobiose, in fact, bears the same relationship to cellulose as maltose does to starch and can be obtained from cellulose by partial hydrolysis.

Lactose

This sugar has been found only in the milk of mammals. It varies from 1.5 to 8 per cent depending upon the species. Human milk contains from 4 to 6.3 per cent and cow's milk about 5 per cent. Based on the annual production of milk (more than 120,000,000,000 lb.), it is estimated that the consumption of lactose in the United States is equivalent to more than one-third that of sucrose. Lactose is obtained from skim milk by removing the casein with acid or rennet and purifying the resultant whey by heating and liming. The clear liquor from these treatments is concentrated in a vacuum pan until crystallization begins. The hot sirup is then transferred to cooling pans and stirred until crystallization is complete. The mush of yellow crystals is dropped into a centrifuge, freed of excess sirup, and washed with cold water. The crude sugar is refined by dissolving, bone-blacking, and recrystallizing. The refined sugar is dried and ground to pass a 200 mesh sieve. The yield of refined sugar averages about one-half the lactose contained in the whey. Lactose production in 1949 amounted to 19,025,000 lb., but this is only a small part of what could be produced if there were sufficient demand for it. Smith and Claborn estimate that at least 2,700,000,000 lb. could be made from available skim milk, buttermilk, and whey. Much of the highly purified lactose is used in infant feeding, and in the manufacture of infant foods and pharmaceutical preparations. Large quantities of pure lactose are also used in the production of penicillin.

Lactose is not very soluble and is almost tasteless. It gives a faint suggestion of sweetness, but this is slight in comparison with the sweetness of glucose or sucrose. A more soluble and sweeter form of lactose can be made by crystallizing the sugar at a temperature above 95°C. This sugar is known as anhydrous beta lactose. The milk sugar of commerce is hydrated alpha lactose. The anhydrous beta lactose appears to be stable for a considerable time at ordinary conditions of temperature and moisture. Because of its greater solubility and sweetening power, it appears that there should be a demand for this product. A more general use of lactose has been advocated for the reason that the ingestion of lactose helps to maintain a healthy condition of the intestinal tract. Although many bacteria are unable to use lactose, others ferment it readily and thus are favored in their development. Among the latter are *L. acidophilus,* a lactic acid-producing microorganism, which is more or less abundant in the intestinal tract. The growth of this desirable organism is favored by an abundance of lactose, and its development results in an acid reaction that checks the growth of the troublesome proteolytic bacteria. Lactose is not fermented by ordinary yeasts.

Lactose reduces Fehling's solution and gives a characteristic osazone, both of which tests indicate the presence of an aldehyde group in its structure. This compound is shown in the following formula:



β-Galactoside part Glucose part

α-Lactose

Note that lactose is a galactoside, not a glucoside, and that the disaccharide linkage is a β-1,4-type. The (potential) aldehyde group is at carbon 1 of the glucose part. In the formula above, the configuration of this reducing group is written as α (—OH down). In β-lactose the configuration around this carbon is reversed, but the structure is otherwise identical to that of ordinary α-lactose.

The mucic acid test is positive with lactose because of the galactose component which is set free by hydrolysis during the test.

THE TRISACCHARIDES, $C_{18}H_{32}O_{16}$

Raffinose

Raffinose is the most important trisaccharide. It is found in small quantities (2–5 per cent) in cottonseed, beet molasses, and manna, and to a less extent in barley, wheat, and other cereals. The amount of raffinose in sugar beets increases considerably as a result of abnormal climatic conditions such as drought and freezing. The sucrose from such beets is hard to crystallize properly as it tends to take on an elongated pointed form. Raffinose is not readily fermented, does not reduce Fehling's solution, and on hydrolysis gives one molecule each of fructose, glucose, and galactose.

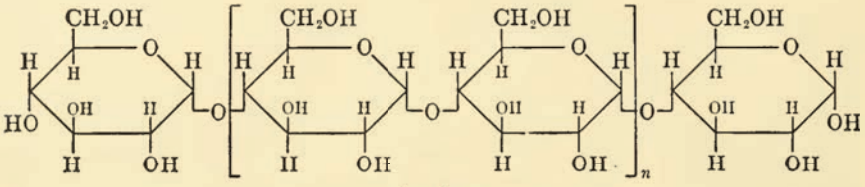
Melezitose

Another trisaccharide that has attracted some notice because of its occurrence in the exudate of the Douglas fir and other coniferous trees is melezitose. In dry seasons the trees become laden with an exudate very rich in this sugar. At such times honey bees gather the material and incorporate it into the honey, where it soon crystallizes and may suggest adulteration. Upon hydrolysis it yields two molecules of glucose and one of fructose.

POLYSACCHARIDES

The polysaccharides are the most complex, as well as the most numerous and abundant, of the carbohydrates found in nature. They are

made up of many molecules of one or more simple sugars combined by glycosidic linkages. For example, a molecule of the polysaccharide *amylose,* a form of starch, consists of about 200–300 glucose units attached to each other by α-1,4-linkages as shown by the following formula:



Amylose

Only four glucose units are shown in this formula, the rest merely being indicated to save space by the *n* outside the brackets. This abbreviation means that the part inside the brackets is repeated *n* times in the complete formula, *n* being about 100–150 maltose units in this particular case. Thus amylose, like all polysaccharides, is a very large molecule, far bigger than the mono-, di-, and trisaccharides so far considered. The molecular weight of amylose is in the range of 10,000–100,000 (no exact value can be determined), whereas sucrose, for example, has a molecular weight of only 342. Polysaccharides in general have molecular weights ranging from a few thousands to several millions.

The example given above, amylose, represents the simplest type of polysaccharide structure, *i.e.,* a long series of simple sugar residues, all of the same kind attached to each other in a single long chain. A second type consists of a branching structure rather than a single chain. Glycogen is an example of this type of polysaccharide. Its structure is indicated by the following diagram, in which each small circle represents a glucose unit:

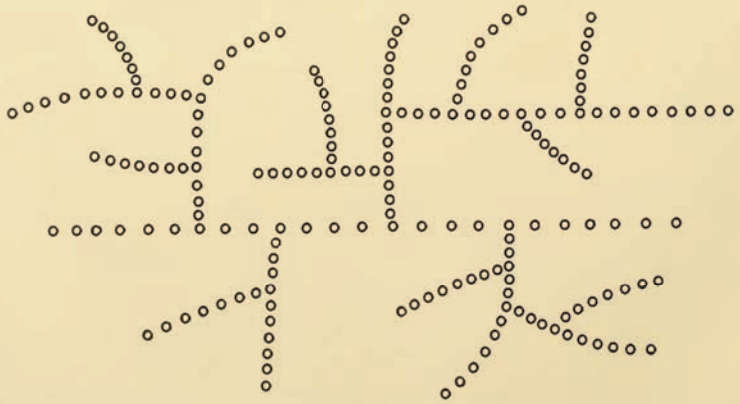


Diagram of glycogen, a branched polysaccharide

A third, and still more complex, type of polysaccharide is made up of several different kinds of simple sugar units, which may be arranged either in a single chain or in a branched structure. These are called *heteropolysaccharides,* whereas those containing only one sugar are classed as *homopolysaccharides.* The chemical formulas of homopolysaccharides are often written in a still more abbreviated form than that of amylose given above. Since one molecule of water is taken away when each glycoside linkage is formed, most of the simple sugar units in the polysaccharide structure (in fact all except those at chain ends) must have the composition of the simple sugar concerned, less one oxygen and two hydrogen atoms. Thus the formula of a pentosan (polysaccharide made up of pentose units) may be written as $(C_5H_8O_4)_x$ and that of a hexosan as $(C_6H_{10}O_5)_x$. These formulas are commonly used because they are compact and easy to write, but they are not precisely correct.

Another important feature of polysaccharide structure is the glycosidic linkage between the monosaccharide residues. This linkage always extends from the reducing group of one simple sugar unit to one of the other carbons of the next unit. This second unit is attached through its reducing group to a third, and so on. Thus no uncombined reducing groups are present in the polysaccharide molecule except the one at the end of the chain (see formula for amylose above). Even branched polysaccharides like glycogen have only one reducing group per molecule. Consequently, polysaccharides as a rule have practically no reducing power.

As a class the polysaccharides are noncrystalline, white solids, which are insoluble or only slightly soluble in water. Probably as a result of this limited solubility they have no appreciable sweetening power. On boiling with dilute solutions of strong acids they are all hydrolyzed, although at greatly differing rates, into the component monosaccharides.

Pentosans $(C_5H_8O_4)_x$

Polysaccharides giving D-xylose or L-arabinose on hydrolysis, that is, the *pentosans,* are very common in nature, especially in the plant kingdom. Most of them, however, are not composed exclusively of pentose residues, but also contain various hexoses, or hexuronic acids, or both, and thus belong to the mixed type of polysaccharides.

The total amount of pentosans contained in various plants is shown in Table 3–5. It will be noted that the largest percentages are found in two main types of plant materials, the plant gums, and the woody or fibrous tissues. Xylan occurs chiefly in wood, straw, leaves, seeds, and vegetables, whereas araban is commonly found in gums and mucilaginous materials. Xylan is frequently associated with glucose in

a double anhydride as gluco-xylan; arabinose may be paired with galactose as a galacto-araban.

Table 3–5

Pentosans in plant materials

[Undried basis]

	per cent
Navy bean	8.4
Corn meal	5.0
Corn (whole)	7.4
Dried peas	7.2
Barley (whole)	11.1
Cottonseed flour	5.6
Beets	1.7
Spinach	1.0
Cabbage	1.0
Wheat bran	22.0
Wheat straw	27.1
Corn fodder	21.8
Corn cobs	35.0
Gum arabic	26.0
Cherry gum	52.0
White pine wood	7.0
Maple wood	21.7

Although the physiological function of pentosans is still obscure, it is doubtful that they are merely the result of an accumulation of waste material. Their very general occurrence in plant material probably indicates that they perform an important function in the life of the plant. Their close relation to cellulose suggests the possibility that they are particularly concerned with structural requirements. Pentosans may also serve as a reserve carbohydrate in the metabolism of the apple tree and thus play an important part in the bearing of fruit.

On hydrolysis, pentosans give pentoses, as is represented by the following equation:

$$(C_5H_8O_4)_x + xH_2O = xC_5H_{10}O_5$$

When substances containing pentosans are boiled with relatively concentrated solutions of mineral acids (HCl, H_2SO_4, or H_3PO_4), the pentosans are hydrolyzed to pentoses, and the pentoses are converted into furfural, as already explained. The red color obtained when furfural reacts with aniline acetate (p. 26) thus serves as a good qualitative test for pentosans. The presence of pentosans in vegetables and whole cereals may be easily demonstrated by holding a piece of filter paper moistened with aniline acetate in the vapors which are evolved when the sample is boiled with 20 per cent hydrochloric acid. By condensing the vapors containing the furfural and adding phloroglucinol, a precipitate

is formed that may be weighed. From this weight the quantity of pentosans can be calculated.

Furfural is also an interesting and important chemical for other reasons. It offers a means of utilizing agricultural waste products such as oat hulls, corn cobs, etc., because these residues contain large amounts of pentosans which can be converted into furfural by a simple, cheap process. The crude furfural so produced is a brownish, oily liquid, which sells for about 10 cents per pound. Large amounts have been used in petroleum refining, and more recently as the starting material for the making of nylon.

The nutritive value of the pentosans is still an unsolved problem. In passing through the digestive tract, considerable quantities disappear. In herbivora from 50–75 per cent of the pentosans, and in man about 15 per cent, appear to be utilized. This utilization must be an indirect one for no digestive enzymes that bring about hydrolysis of pentosans are known to occur in higher animals. It is assumed that the bacteria of the intestine break down the pentosans into soluble products such as acetic and lactic acids, which are then absorbed and utilized. Considering the large amount of pentosans consumed by herbivorous animals, it seems that such a fermentation must be very rapid.

Hexosans $(C_6H_{10}O_5)_x$

Starch is the most important food carbohydrate. It contributes more calories to the usual diet of human beings than any other single substance. Ordinary starch, as it is found in plants, is a mixture of *amylose* and *amylopectin*. Usually there is a much greater proportion of the amylopectin. For example, corn starch and potato starch each contain about four-fifths amylopectin and one-fifth amylose. The so-called waxy corn starch is almost all amylopectin. The two fractions can be separated by dispersing the crude starch in hot water saturated with butyl alcohol. On cooling slowly, the amylose separates as a semicrystalline precipitate, which is easily removed. The amylopectin can then be recovered from the solution.

Both amylose and amylopectin are polysaccharides made up of anhydroglucose units attached to each other by α-1,4-linkages. Amylose, as explained on p. 50, is a linear-type polysaccharide, consisting of a long, unbranched chain of about 200–300 glucose units. On the other hand, amylopectin has a branched structure somewhat similar to that of glycogen (see diagram on p. 50). At the point of branching, α-1,6-linkages are present. The molecular weight of amylopectin is thought by many investigators to be at least 500,000, which corresponds to 2000–3000 glucose units in the molecule.

Amylose is less soluble in water than amylopectin. It gives a clear

blue color with iodine, whereas amylopectin gives a violet-blue color. This color is attributed to the branched structure of amylopectin. Glycogen, which is even more highly branched than amylopectin, gives only a red-brown color in the iodine test. Neither component of starch shows any reducing power unless very refined tests are employed. Thus the usual Fehling's test is entirely negative with native starch. However, soluble starch, which is made by subjecting starch to a mild acid and heat treatment, does give a positive Fehling's test. This effect indicates that the process of making the starch soluble has also resulted in some decomposition and liberation of aldehyde groups.

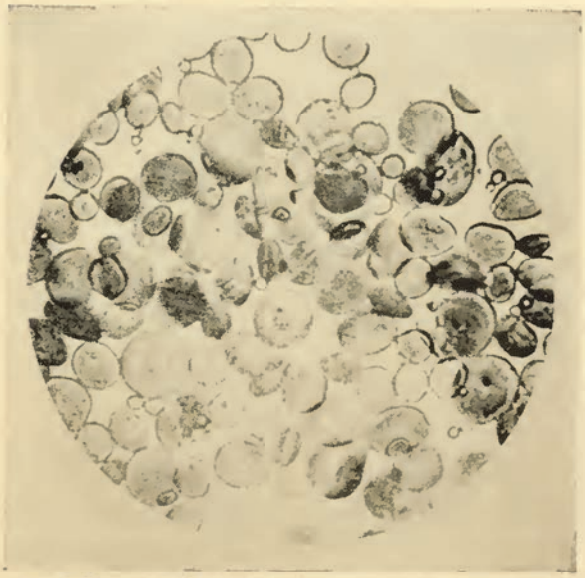
Starch usually contains a few hundredths of a per cent of phosphorus, probably as a result of the fact that it is formed in plants from glucose-1-phosphate. Fatty acids (for example, oleic, linoleic, and palmitic) have been found in various cereal starches, but it is probable that they are present as impurities rather than as actual constituents of the starch molecules since they can be removed by extraction with boiling methyl alcohol.

Starch is found in almost all chlorophyll-bearing plants. It is especially abundant in the common cereals (wheat, rye, oats, and rice); it makes up from 60 to 80 per cent of the seed. Also peas and beans may contain 50 per cent of starch. In certain oily seeds (*e.g.*, cottonseed, flaxseed, and soybeans) fats, instead of starch, form the storage material. As a general rule seeds grown in the tropical regions are oil bearing, whereas those of the temperate regions are high in starch. Many tubers, such as the potato, are made up largely of starch. When unripe, the apple and banana contain considerable quantities of starch. While these fruits ripen, the starch is converted into sugar. The changes in cereals during the ripening period are just the opposite of those that occur in the apple and banana. Sweet corn is a striking example of a plant that contains an abundance of sugar when the kernals are young, but only a little sugar and much starch when the seed is mature.

In nature the starch molecules are built up to form a larger aggregate called a granule. Every plant has its own characteristic starch granules, with or without particular markings (see Figs. 3–2 to 3–5). For example, the potato starch granule is large, oval, and marked by concentric lines arranged around a point called the hilum, at one end of the granule. That of wheat starch, on the other hand, is smaller and spherical in shape, without any particular markings. Oat starch is made up of a number of particles and forms what is known as a compound starch granule. The different fragments fit together in the form of a mosaic. Because of this distinctiveness in appearance, it is comparatively easy to determine the kind of starch that is present in a food material. Microscopic examination of spices and flours is of great help in determining whether or not these materials have been adulterated by the addition

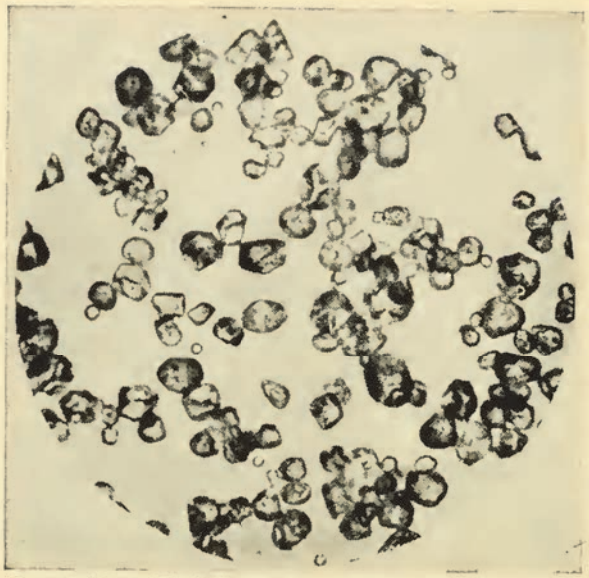
From Reichert, *The Differentiation and Specificity of Starches*. Courtesy of the Carnegie Institution of Washington.

Fig. 3–2. Starch granules from potato.



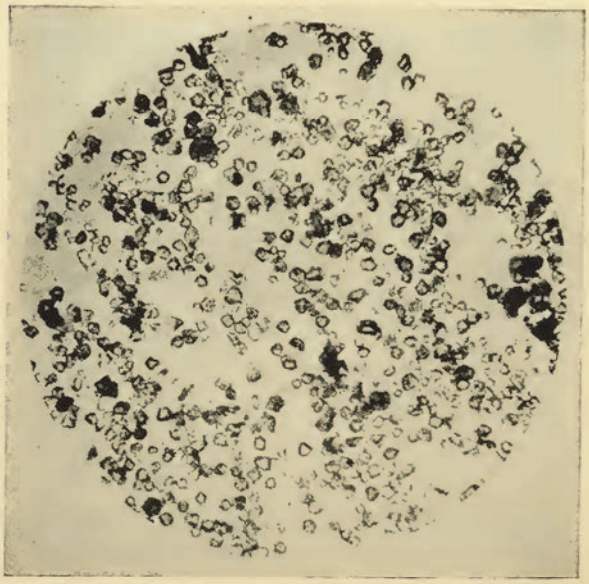
From Reichert, *The Differentiation and Specificity of Starches*. Courtesy of the Carnegie Institution of Washington.

Fig. 3–3. Starch granules from wheat.



From Reichert, *The Differentiation and Specificity of Starches.* Courtesy of the Carnegie Institution of Washington.

Fig. 3–4. Strach granules from corn.



From Reichert, *The Differentiation and Specificity of Starches.* Courtesy of the Carnegie Institution of Washington.

Fig. 3–5. Starch granules from rice.

of foreign substances whose starch granules are different from those of the pure materials.

Commercial starch is usually made from corn or wheat in the United States and from potatoes in Europe. Other commercial starches are sago, tapioca, and arrowroot. The preparation of starch in the United States is associated with the manufacture of numerous other products such as corn oil, gluten feed, and glucose sirup. For details concerning the process of manufacture, see the industrial chemistries listed.

Starch is insoluble in cold water, but at higher temperatures (52° to 72°C., varying with the kind of starch) the starch grains absorb water, swell, and finally form a sticky paste or opalescent semisolution. The absorption of water and swelling of starchy material on heating is well illustrated by the changes in volume and viscosity that rice undergoes when it is boiled.

Like other polysaccharides, starch is hydrolyzed by boiling in dilute mineral acid solutions. If the boiling is continued long enough, the starch is converted entirely into glucose, as shown in the following equation:

$$\underset{\text{Starch}}{(C_6H_{10}O_5)_x} + xH_2O \xrightarrow[100°]{H^+} \underset{\text{Glucose}}{xC_6H_{12}O_6}$$

However, the large starch molecule does not split up all at once into glucose but passes through a number of intermediate stages. At first only a few of the glucosidic linkages are hydrolyzed so that large fragments of the original molecule are formed. This renders the starch water-soluble. More hydrolysis leads to smaller fragments of the starch molecule, which are called *dextrins*. These in turn are broken down into maltose and finally glucose.

The manufacture of sirup from starch involves its hydrolysis by acid with glucose and maltose as the principal products, together with a considerable quantity of dextrin. The hydrolysis is commonly carried to the point at which iodine no longer gives a color with the hydrolysis mixture. The composition of commercial corn sirup, as calculated from a number of analyses reported by Fetzer, Evans, and Longenecker, is as follows:

	per cent
Water	18.48
Dextrins	28.11
Maltose	36.33
Dextrose	16.78
Crude protein	0.05
Ash	0.25

Starch, dextrins, and glycogen are also hydrolyzed by various starch-splitting enzymes called *amylases*. This process differs from acid hydrolysis in that the chief product formed is maltose rather than glucose:

$$\underset{\text{Starch, dextrins, or glycogen}}{(C_6H_{10}O_5)_x} + \tfrac{x}{2}H_2O \xrightarrow{\text{amylase}} \underset{\text{Maltose}}{\tfrac{x}{2}C_{12}H_{22}O_{11}}$$

This conversion, however, is generally not complete because the amylases can attack only α-1,4-linkages between glucose units. Thus amylose is completely hydrolyzed into maltose, but the breakdown of amylopectin stops when α-1,6-linkages (branch points) are reached. This discontinuance results in the formation of *limit dextrins* which consist mostly of glucose tri- and tetrasaccharides, each containing at least one α-1,6-linkage. The amount of limit dextrins formed is usually about 10 to 20 per cent of the amount of starch hydrolyzed.

The amylase enzymes have received various common names according to the place where they are found. Thus the amylase of saliva is called *ptyalin;* that in pancreatic juice, *amylopsin;* and the very active amylases present in sprouting cereal grains and other plant sources are frequently named *diastase*. *Takadiastase* is another amylase preparation, obtained from a mold fungus, *Aspergillus oryzae*, which has long been used in the Orient for making certain fermented foods. However, in all of these variously named preparations there are only two basically different types of amylases, which are designated merely as *alpha* and *beta* amylase, respectively. The manner in which each of these attacks starch is explained in detail in Chap. 10.

The removal of starch from textiles and starched goods by means of amylase is an application of enzyme action to an industrial problem. The fabric is not attacked as when alkali or acid is used, and hence the enzyme is to be preferred to other means of starch removal. Many textile mills now make use of such commercial amylase preparations.

Dextrins

As already noted, dextrins are intermediate products in the hydrolysis of starch to maltose. They differ from starch by being soluble in cold water and from maltose by being insoluble in alcohol. They are also found as native products in the roots, stems, and leaves of many plants. Starchy seeds in the resting stage contain a small percentage of dextrin and when germinating, a large amount.

Dextrins are formed from starch in many household operations requiring heat: baking of bread, cake, etc., and ironing of starched clothes. The toasted breakfast foods, corn flakes, shredded wheat, puffed rice, and so on, contain considerable quantities of dextrin produced by the heating of these foods.

Commercial dextrins are made by heating starch with or without the addition of acid. If acid is used, a lower temperature is sufficient to

bring about the partial hydrolysis of the starch. "British Gum" is one of the important commercial dextrins. Dextrins are widely used as adhesives on postage stamps, envelopes, and textiles. Mucilage and other industrial pastes are composed largely of dextrin. In the manufacture of cotton cloth, the material is sized with dextrin to make possible the printing of the pattern. The candy industry uses large quantities of dextrin to give a smooth texture to the product.

The starch-splitting enzymes, ptyalin, amylopsin, and diastase, act also on dextrins and form the same end product as from starch, namely, maltose. Since dextrins include a number of degradation products of starch, it is not surprising that they differ in their response to the iodine test. Some are colored blue-violet, others red-brown, and yet others are not colored at all by iodine.

Glycogen

Glycogen, or as it is sometimes called, animal starch, is the chief form in which carbohydrates are stored in the animal body. It is found most abundantly in the liver and muscles, but has also been isolated from bone, blood, skin, and many other tissues. It seems to be present in all animal cells. The amount fluctuates within wide limits. Hunger and severe muscular work greatly deplete the supply of glycogen, whereas liberal feeding with carbohydrate foods greatly increases it. By feeding, the glycogen content of the rabbit's liver has been raised to 27 per cent of the total weight of the liver. In the dog, under the same conditions, a 17 per cent glycogen content of the liver has been found. In man it is estimated to reach as high as 10 per cent on a high carbohydrate diet. Under usual conditions the liver of an animal contains from 1.5–4.0 per cent. Other animal tissues have been found to contain the following percentages of glycogen: muscle, 0.5–0.9; skin, 0.1–1.7; bone, 0.2–1.9; blood, 0.007–0.016. The percentage of glycogen varies in the same kind of tissue of different animals, in the different muscles of the same animal, and in the different parts of the same muscle.

Like amylopectin, glycogen is believed to consist of branched chains that form a macromolecule containing about 2400 glucose residues. Such a molecule would have a molecular weight of about 400,000. The length of the individual chains in glycogen appears to be shorter than in starch and is thought to contain from 12 to 18 glucose units instead of 24 to 30 units as reported for starch.

A so-called plant glycogen has been found in several plants, molds, yeasts, etc., which possesses many of the chemical properties of animal glycogen, for example, iodine reaction, but is unlike it in certain other aspects, such as optical activity.

Glycogen is a snow-white powder readily soluble in water, with which

it forms an opalescent colloidal solution. With iodine, glycogen gives a red-brown color, which is made somewhat more pronounced by the addition of sodium chloride. It does not reduce Fehling's solution. It is hydrolyzed by the action of dilute acids to maltose, and finally to glucose. Like starch, glycogen is not fermented by yeast, but is readily hydrolyzed by starch-splitting enzymes. Diastase, ptyalin, and amylopsin convert it into maltose.

Bacterial dextrans

The dextrans [1] are polysaccharides produced by several species of bacteria, notably *Leucanostoc mesenteroides*. Composed entirely of glucose, they are high molecular weight (several million), water-soluble substances, which can be precipitated from aqueous solutions by adding an equal volume of alcohol. The glucose units are attached to each other by α-1,6-linkages in chains which have many branches. At the branch points, α-1,4-linkages occur. The structure is thus the reverse of that of glycogen and amylopectin, where the chains are held together by α-1,4-linkages, and α-1,6-links are found only at branch points.

Bacterial dextrans, like other glucosans, can be hydrolyzed with acids to form glucose. Dextran degraded by partial hydrolysis to an average molecular weight of about 100,000 has been used in the form of a 6 per cent solution in 0.9 per cent saline solution as a substitute for plasma in blood transfusions. Although by no means a complete substitute for plasma or whole blood, such solutions do have considerable value for body fluid replacement in cases of severe burns, shock, blood loss, and the like. One of the main problems in such cases is to prevent further loss of fluid from the body, and this can only be done if the fluid used for the transfusion contains a nondiffusible solute which gives it an osmotic pressure similar to that normally caused by the blood serum proteins. The dissolved substance must have about the right molecular weight, must remain in the blood for a day or two, must not cause too great viscosity, and must not be toxic or produce any undesirable side effects. Partly hydrolyzed dextran is one of the most satisfactory materials of a number which have been investigated for this purpose.

Cellulose

Cellulose consists of an unbranched chain of D-glucose units joined by β-1,4-linkages. Thus it closely resembles amylose except for the β-linkage and a much higher molecular weight. Many efforts have been made to determine the number of glucose units in the chain, and values ranging all the way from a few hundred to several thousand have been

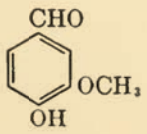
[1] Do not confuse with dextrins.

reported (compare with amylose, p. 50). Probably the higher figures are more nearly correct for intact cellulose as it actually exists in plants.

The woody and fibrous tissues which provide strength and rigidity for plants, as bones do for animals, are composed of a mixture of cellulose with several other polysaccharides (*hemicelluloses* and *cellulosans*) and a noncarbohydrate material, *lignin*. Cotton fibers are an exception to this statement since they consist of practically pure cellulose (over 98 per cent).

From an industrial and economic standpoint cellulose is the most important of all the carbohydrates (see Table 3–1, p. 20). Cotton and linen goods, rayon, paper and pulp products, rope, twine, and other cordage materials are composed almost entirely of cellulose. The largest single source is wood, either in its natural form or in the form of paper and pulp products. Wood contains, on the dry basis, about 60–70 per cent of carbohydrates and 20–30 per cent of lignin. About half of the carbohydrate fraction consists of true cellulose. The process of paper-making is essentially a matter of separating the cellulose from the lignin, hemicellulose, and other constituents of wood. Pressure-cooking the wood, in the form of chips, at 130–175°C., with water containing such chemicals as calcium bisulfite plus sulfur dioxide (sulfite process) or sodium hydroxide plus sodium sulfide (Kraft process), dissolves the lignin and most of the hemicelluloses. The insoluble fiber or "pulp," consisting of most of the cellulose plus smaller amounts of other resistant polysaccharides, is separated from the water solution, called "waste liquor," and either rolled into sheets to make paper or used as a source of crude cellulose for other industrial purposes (see below). During the years 1947–1950 wood pulp was produced in the United States at the rate of about 12,000,000 to 15,000,000 tons annually.

Disposal of the enormous quantities of waste liquors, produced as a by-product of the pulp and paper industry, is still an unsolved challenge to chemists. The sugars present can be fermented to produce alcohol, lactic acid, or yeast, but only a small portion of the total is so utilized. Heating with strong alkali converts 10 to 20 per cent of the lignin into vanillin, a component of vanilla. Unfortunately the use of vanillin for flavoring offers a market for only a tiny fraction of the lignin available.



Vanillin

Mercerized cloth, named after John Mercer who originated the process, is obtained by treating cotton cloth with alkali and subsequently washing and drying the cloth. The individual fibers become thicker and shorter.

Their strength becomes approximately 20 per cent greater, their affinity for dyes is greatly increased, and a smooth glossy surface is produced.

Synthetic yarn, also known as rayon or artificial silk, is a cellulose product that has achieved great importance since World War I. In 1949 nearly 500,000 tons were produced in America, while world production in 1947 was twice this figure. The rapid progress of this industry in the United States is indicated by the fact that only 63,500 tons of rayon were produced in 1930. Synthetic yarns are made from xanthate, acetate, nitrate, and cuprammonium compounds of cellulose. Of the four, the most important is the type produced by the xanthate or viscose process, which uses sodium hydroxide and carbon disulfide as the chemicals for dissolving the cellulose. Although the term "rayon" was originally applied solely to the product of this process, the Federal Trade Commission has ruled that all manufactured textile fibers of cellulosic origin shall be included in the term.

The cellulose products, instead of being spun as a thread, may be produced in the form of a sheet or film. Cellophane, a colorless transparent material which is extensively used for wrapping purposes, is made by the viscose process, in which the cellulose is regenerated in the form of a sheet of varying thickness. Motion picture films and glass substitutes, which allow the ultraviolet rays of the sunlight to pass through, are other examples of sheet cellulose products. "Safety glass" used in automobiles usually consists of a sheet of glass on each side of a layer of cellulose acetate. Cotton lacquers, such as Duco, which in recent years have come into extensive use for the surfacing of automobiles and furniture, contain as one of their essential constituents some ester of cellulose, usually the nitrate or acetate.

Nitrate esters of cellulose are used for many purposes. Cellulose trinitrate $[C_6H_7O_2(NO_3)_3]_x$ is the well-known explosive, guncotton. The less completely nitrated cellulose is known as pyroxylin and is extensively used in the manufacture of plastics, such as celluloid. Celluloid is a mixture of two parts pyroxylin and one part camphor. The strongly combustible nature of all celluloid materials is due to the presence of the nitrate groups. Collodion is a solution of pyroxylin in alcohol and ether. When this solution is painted over a wound, the alcohol and ether evaporate leaving a thin membrane, "new skin." When used in manufacture of artificial silk, cellulose nitrate must be denitrated to render it noninflammable. This is accomplished by treatment with an acid sulfide, for example, sodium acid sulfide (NaHS).

Cellulose is not acted upon by the enzymes of the digestive tract of vertebrates. However, certain snails and insects secrete an enzyme, cellulase, which is capable of digesting cellulose. Cows, sheep, and horses consume large quantities of cellulosic material, and a large proportion of this material (50 to 85 per cent) disappears from the digestive

tract. Since no cellulose-digesting enzyme is known to be secreted by these animals, it is assumed that the hydrolysis is brought about by the action of bacteria. The products formed by such bacteria—acids, or possibly even glucose—may be absorbed and thus serve as sources of energy to the animal. Although cellulose is of no importance to man as a source of energy, its presence in the digestive tract may serve a useful purpose in giving bulk to the food and may assist in the elimination of food residues. However, there is considerable difference of opinion regarding the value of bulk in the diet.

On complete hydrolysis pure cellulose gives only glucose. Soft woods (spruce, pine, fir, etc.) give about 50 per cent of glucose and about 10 per cent of xylose and other sugars. However, it is not practicable to make glucose from wood and other cellulosic materials because of the difficulties encountered in purifying the sugar. In Europe, wood sugar solutions are fermented for production of ethyl alcohol and yeast on a commercial scale. Such liquors have also been evaporated and used as feed for cattle.

Fructosans

Polysaccharides that upon hydrolysis yield fructose are reported to be fairly widespread in plants. Eight fairly well-defined members of this group of polysaccharides have been described. The best known are *inulin* and the bacterial *levan* produced by *Bacillus subtilis*. Inulin consists of about 30 D-fructose residues linked from carbon 2 of one residue to 1 of the next. It is abundant in the roots of the Jerusalem artichoke, dahlia, sunflower, dandelion, and many other plants. The amount varies with the season of the year. It has been proposed that inulin be manufactured from the Jerusalem artichoke, since this plant produces a very large tonnage per acre, and that the inulin be converted into levulose by acid hydrolysis. However, up to the present time this process has not been attempted on a commercial scale.

Inulin is a white powder readily soluble in hot water but only slightly soluble in cold water. It gives no color with iodine solution and is easily hydrolyzed with dilute acids. It is not acted upon by diastase, ptyalin, amylopsin, or any known body enzyme. It is not fermented by ordinary yeast, but is easily broken down by many bacteria.

The bacterial levan of *B. subtilis* is similar to inulin in its properties, but is made up of D-fructose residues united at the 2 and 6 positions.

Galactans

Anhydrides of the sugar, galactose, are known as galactans. They are frequently found in combination with arabinose as a double compound,

galactoaraban. Galactans are found in peas, beans, and certain other legumes. They are not hydrolyzed by the enzymes of the digestive tract; consequently their nutritive value can be only indirect.

Mannosans

These polysaccharides both in the simple form and in combination with the anhydrides of other sugars, for example, fructose and galactose, have been found in yeast, mushrooms, seeds, nuts, fruits, berries, leaves, and practically all plant tissues. They are especially abundant in the ivory nut, coffee bean, and carob bean. The best known members of this class are ivory nut mannan and salep mannan. When salep, a meal obtained from the dried tuberous roots of various orchids, is extracted with water and alcohol added to the extract, the mannan precipitates as a white powder. On acid hydrolysis only D-mannose is formed. The polysaccharide is made up of the D-mannose residues attached by β-1,4-linkages in a single, unbranched chain. Ivory nut mannan is similarly constituted, but is insoluble in water.

Although certain molluscs and crustaceans secrete enzymes that hydrolyze mannans, no digestion of these carbohydrates is brought about by the digestive enzymes of higher animals.

Chitin

The polysaccharide, *chitin,* is widely distributed in nature, being found in the exoskeletons of many invertebrate animals, as well as in certain plants and fungi. Typical examples of its occurrence are the cuticle of insects and the shells of crabs and lobsters, where it makes up about one-fourth to one-half of the dry weight. It functions as a highly resistant protective substance and, together with protein and mineral matter, gives strength and rigidity to the organism. Chitin is remarkably insoluble in all ordinary solvents and resistant to alkaline hydrolysis, although it can be hydrolyzed by long heating with strong acid.

Chemically, chitin consists of N-acetyl-D-glucosamine residues linked through the 1,4-positions into a linear chain several hundred units long. It is thus one of the very few major carbohydrates in nature which contains nitrogen.

Pectin

This carbohydrate is contained in the water extract of many fleshy fruits. On addition of acid and sugar in proper concentrations, pectin forms a gelatinous mass well known as jelly. The mother substance existing in the plant, designated as protopectin, is considered by many

investigators to be a member of the group of hemicelluloses. It is very widely distributed in nature, being found in varying quantities in most fruits, vegetables, and roots. Ripening of the fruit, or action of acid and heat, converts the insoluble protopectin into soluble pectin. This change is well illustrated in jelly making, where boiling the fruit is necessary to get the maximum amount of pectin. However, prolonged boiling converts the pectin into hydrolysis products that do not have the property of jelling. In the ripening of fruits, enzymes bring about the hydrolysis of pectin, and, hence, overripe fruits are not suitable for making jelly.

Structurally, pectin is a polysaccharide consisting of a long chain of D-galacturonic acid units (pp. 38, 39) in which some of the carboxyl groups are united with methyl alcohol through an ester linkage ($-COOCH_3$). The galacturonic acid units are joined through carbons 1 and 4, as are the glucose units in starch, glycogen, and cellulose. Opinions differ, but it appears that any arabinose or galactose obtained by hydrolysis of pectin preparations comes from associated polysaccharides rather than from the pectin itself.

The manufacture of commercial pectin to aid the housewife in compelling unwilling jellies to jell, or in making jellies from fruits that contain little or no pectin, has become an industry of considerable proportions. A well-known product of this kind is "Certo," which is made from apple pomace. Dry pectin has recently been developed from apples and lemons. On the basis of dry matter, apple pomace and lemon pulp contain about 20 and 35 per cent, respectively, of pectin. Rinds of "cull" lemons are used for this purpose and furnish a much larger supply of raw material than can be utilized at the present time. Sugar beet pulp contains on the dry basis about 25 per cent of pectin and offers an almost unlimited supply of raw material for the manufacture of pectin.

Sugar, acid, and pectin are necessary to form a gel. These three ingredients may be varied within rather wide limits, but a jelly of good texture contains about 60–70 per cent sugar, 1–2 per cent acid (expressed as tartaric and equivalent to pH 3.2–3.5) and 0.5–1.0 per cent pectin.

Closely related to pectin is the acidic polysaccharide, alginic acid, which is obtained from marine algae. Like pectin, it has the property of holding large amounts of water in a colloidal gel. For this reason it is used, in the form of its sodium salt, as a stabilizer in ice cream and other foods, and in cosmetics. Because it is capable of forming hard, resistant, surface films, it is also used in making special grades of paper, cloth, and printer's ink. Chemically, alginic acid is composed of D-mannuronic acid residues attached by β-1,4-linkages in an unbranched chain structure. It is remarkably resistant to hydrolysis, even when exposed to strong acid

or alkali. Since no body enzymes can digest alginic acid or pectin, they have no food value.

HETEROPOLYSACCHARIDES

Most of the carbohydrates in this group are too complex and too imperfectly known to be included in an elementary book. Examples of several types have been given in connection with the classification of carbohydrates (p. 21), and several others have been mentioned briefly in the sections on wood (p. 61), pentosans (p. 52), and galactans (p. 63). A few heteropolysaccharides of special importance are discussed in more detail below.

Heteropolysaccharides from plants

The *hemicelluloses* are one of the most important subgroups of this large, rather poorly-defined, class of carbohydrates. As indicated on p. 61, they are present in fibrous and woody plant tissues, where they are combined with cellulose and lignin to form the cell walls. The hemicelluloses are distinguished from cellulose by the facts that they are acidic substances and are made up quite largely of D-xylose units, although other sugars (D-galactose, L-arabinose, D-glucose, D-mannose) may also be present in smaller amounts. Their acidic properties arise from the presence of a hexuronic acid, probably D-glucuronic acid, which is also one of the component units. Ordinary wood pulp contains considerable amounts of hemicelluloses.

The *plant gums* such as cherry gum, mesquite gum, gum arabic, and gum tragacanth are neutral salts of complex polysaccharide acids composed of residues of hexoses, pentoses, methyl pentoses and uronic acids. The uronic acid in nearly all plant gums is D-glucuronic acid, and the sugars commonly present include D-galactose, D-mannose, L-arabinose, D-xylose, L-rhamnose, and L-fucose. The complete structures have not been worked out. Plants produce such gums when they are injured, no doubt as a protective mechanism.

Another group of mixed-type polysaccharides, widely distributed in plants, form viscous, colloidal solutions in water and hence are called mucilages. These are roughly divided into neutral, acidic, and sulfate-containing groups. An example of a neutral mucilage is gum ghatti, which on hydrolysis gives rise to 16 per cent of D-galactose and 84 per cent of D-mannose. The majority of the mucilages in seeds are of the acidic type, with the acidity being due in all cases to D-galacturonic acid residues. Sea weeds contain a large number of mucilages, nearly all of which contain sulfate groups (*i.e.*, some of the hydroxyl groups of the sugar residues present are esterified with sulfuric acid). D-Galactose

is the chief sugar obtained on hydrolysis. The best known sea weed mucilage is agar, which is widely used in bacterial culture media because of its property of forming gels.

Heteropolysaccharides of animals

Several carbohydrates of this type occur in small amounts in the animal body. *Hyaluronic acid*, a polysaccharide composed of equimolar portions of D-glucosamine acetate and D-glucuronic acid residues, forms a viscous, gel-like material present in connective tissues, eyes (aqueous and vitreous humor), joints (synovial fluid), and various other organs. It functions as a cementing substance between the cells of connective tissue (so-called "ground substance") and, because of its viscosity, resists penetration by foreign matter, *i.e.*, infection by bacteria. Hyaluronic acid is attacked and liquefied by an enzyme, *hyaluronidase*, which is present in some bacteria, in certain animal tissues, and in the poisonous secretions of many reptiles and other animals. This enzyme, to the extent that it is present, contributes to the rapid spread of toxic agents throughout the body; it is therefore of great medical interest.

Chondroitin sulfate, a major component of cartilage, is a heteropolysaccharide made up of D-glucuronic acid and D-galactosamine acetate residues, with some of the hydroxyl groups esterified by sulfuric acid. In the living animal it is probably attached through its carboxyl and sulfate groups to the amino groups of proteins. *Mucoitin sulfate*, present in mucosa (*e.g.*, stomach mucosa and gastric juice), is similarly constituted except that it contains D-glucosamine acetate residues.

Another animal polysaccharide of considerable importance is *heparin*, a natural anticoagulant (inhibitor of blood coagulation), which occurs in the liver, muscles, and other organs of the body. The component building blocks of heparin, as shown by their formation on complete hydrolysis, are D-glucuronic acid, D-glucosamine, and sulfuric acid. It is noteworthy that no acetic acid is involved since in the other animal polysaccharides, which contain amino sugars, the amino group is acetylated (*i.e.*, combined with acetic acid to form the acetylamino group, $-NHCOCH_3$). Furthermore, heparin contains more sulfate residues than most of the other sulfate-containing carbohydrates discussed above. According to Wolfrom and co-workers the repeating unit in heparin is a tetrasaccharide composed of two residues of glucosamine and two of glucuronic acid plus five sulfate radicals. An unusual feature of the heparin structure is the union of the amino group of each glucosamine unit with a sulfate radical to form a sulfamic acid group, $-NHSO_3H$. The sulfuric acid here takes the place of acetic acid in other animal polysaccharides.

Immuno-polysaccharides

Certain polysaccharides, unknown until fairly recently, doubtless play a role of greater importance in our lives than many of the related compounds with which we are more familiar. These are the immuno-polysaccharides, which pneumococci, streptococci, tubercle bacilli, and many other types of bacteria synthesize and transfer to the solution, blood as well as culture media, in which they grow. Each type produces a characteristic chemical compound or "specific soluble substance," the presence of which in the blood stream of an individual stimulates production of antibodies, and thus builds up immunity to a given disease. Since these polysaccharides are "type specific," it is apparent that each must differ chemically from the other. D-Glucose, D-glucosamine, and various sugar acids have been identified among the hydrolysis products of these immuno-polysaccharides. A recent contribution to immuno-chemistry is the discovery that appropriate synthetic organic compounds containing glucuronic and galacturonic acids, as well as the specific polysaccharides of bacterial origin, may evoke production of antibodies and thus establish immunity to a particular disease in an experimental animal. These results show the great importance of the sugar acids and throw new light on the structure of the specific polysaccharides.

REVIEW QUESTIONS ON CARBOHYDRATES

1. Define: carbohydrate, simple sugar, uronic acid, heteropolysaccharide, asymmetric carbon atom, optical rotation, desoxysugar, glycoside.

2. How many substances of each of the following types can theoretically exist: aldopentose, 2-ketohexose, aldohexose? Explain.

3. Name four disaccharides made up of glucose units only and explain how they differ from each other.

4. Give two commercial sources of (1) sucrose, (2) cellulose, (3) starch; one commercial source of (4) glucose, (5) lactose. Briefly outline the procedure in the manufacture of sucrose from one of the above sources. Outline the steps in the manufacture of glucose.

5. Explain the terms: (1) invert sugar, (2) hydrolysis, (3) sucrase, (4) pentosan, (5) mercerization, (6) celluloid.

6. Write equations and name the products in: (1) the photosynthesis of glucose, (2) the hydrolysis of sucrose, (3) the digestion of starch by saliva.

7. What are the chief carbohydrates in (1) honey, (2) fruits, (3) liver, (4) blood, (5) milk, (6) condensed milk, (7) cereals? Approximately what is the percentage of the carbohydrate named in each case?

8. Explain the terms: (1) pentose, (2) photosynthesis, (3) pectin, (4) dextrin, (5) beta lactose, (6) cellophane, (7) rayon.

9. Write equations and name the products in: (1) the hydrolysis of starch by acid, (2) the mucic acid test for galactose, (3) a positive Fehling's test.

10. By means of graphic formulas explain how glucose, galactose, and fructose may all have the same molecular formula, $C_6H_{12}O_6$, and still be different chemical compounds. Explain why sucrose does not reduce Fehling's solution, while maltose does.

11. Give another example of two substances that have the same molecular formula and explain the differences in their structure.

12. Name three carbohydrates found in animal material, telling where each is found and approximately how much of each is present.

13. Discuss the occurrence of pentose-yielding substances in nature. What becomes of these substances? What commercial value do they have?

14. Explain the changes that occur when fruits are boiled to make jelly. What happens when the fruit is boiled too long?

15. Name some important commercial products made from cellulose.

16. What is rayon? Name the principal cellulose compounds used in its manufacture.

17. Name all the carbohydrates that are suitable for food purposes. Name those not digested by the digestive enzymes of higher animals. Name an animal that can digest cellulose.

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Chapter 4

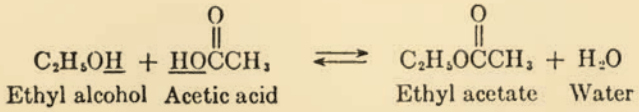
LIPIDES (FATS AND RELATED SUBSTANCES)

In every-day use the term fat has a fairly definite meaning. It suggests such familiar substances as butter, lard, tallow, olive oil, cottonseed oil, and so on. However, if the distribution of fats in nature is studied more closely, it soon becomes apparent that fats exist in less obvious and less easily characterized combinations. Although the common fats are essentially combinations of glycerol and fatty acids, many other constituents are contained in fats and fat-like substances. Because of this heterogeneity no very satisfactory classification of the fats has yet been worked out. Perhaps the best one yet developed is that by Bloor who bases his classification on three points: (1) solubility (*e.g.*, insoluble in water, soluble in ether, chloroform), (2) structure, *i.e.*, esters of the fatty acids, either actual or potential, (3) utilization by living organisms. From Bloor's classification it is evident that fats or lipides are essentially ester combinations that yield various products on hydrolysis. The table on page 73 gives examples of the different classes of lipides and the products formed by hydrolysis. This table gives a general view of the lipides as a whole and should be used as a guide to which additions are to be made as each class of lipides is studied more intensively.

ESTERS

Definition

Since the lipides consist, for the most part, of esters, it is important for the student to understand clearly just what is meant by the term ester. An ester is a substance formed by the chemical reaction of an alcohol with an acid, whereby a molecule of water is eliminated. The formation of a simple ester is represented by the following equation:



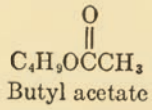
The underlined H of the alcohol and HO of the acid become separated from their previous points of attachment and unite to form H_2O, while the remaining portions of the acid and alcohol combine to form the ester as indicated. The chemical formula of any ester therefore follows directly from the formulas of the alcohol and acid of which it is composed. The name of any particular ester is derived similarly. Thus in the above equation the product is called ethyl acetate. An ester prepared from methyl alcohol and lactic acid would be called methyl lactate, and so on.

Preparation

The actual preparation of esters in the laboratory is carried out, in general, by warming the chosen alcohol and acid together with a small amount of a strong mineral acid, such as sulfuric or hydrochloric, which serves as a catalyst. The process is called esterification. Since esterification reactions are, in general, reversible, removal of the water as it is formed often helps to secure a good yield of the desired ester. It is obvious that a very large number of different esters may be prepared from the various alcohols and acids (particularly organic acids) that are known and are available.

Properties of esters

Many of the simpler esters are liquids that possess pleasant, fruity odors and hence are used to some extent as artificial flavoring essences. More complex esters are found very abundantly and widely distributed in nature, *e.g.*, in fats, waxes, and other lipides, as explained below. By far the most important industrial use of synthetic esters is based on their properties as solvents. Automobile lacquers, for example, are prepared by dissolving pyroxylin, a pigment, and certain other ingredients in a suitable ester such as butyl acetate:



$C_4H_9OCCH_3$

Butyl acetate

All esters may be broken down into their acid and alcohol components by hydrolysis:

$C_4H_9OCCH_3 + H_2O \longrightarrow C_4H_9OH + HOCCH_3$

Butyl acetate Water Butyl alcohol Acetic acid

It will be noted that this reaction is the reverse of esterification. The hydrolysis may be brought about with the aid of an enzyme, if one is

Table 4–1

Classes of lipides and their hydrolysis products

Lipide	*Hydrolysis Products* *	
	Alcohol (name and formula)	*Acid and other products* (name and formula)
I. Simple lipides:		
1. True fats (in butter, lard, oils)	Glycerol, $C_3H_5(OH)_3$	Stearic, $C_{17}H_{35}COOH$ Oleic, $C_{17}H_{33}COOH$
2. Waxes (in beeswax)	Cetyl, $C_{15}H_{31}CH_2OH$	Cerotic, $C_{25}H_{51}COOH$
II. Compound lipides:		
1. Phospholipides, *e.g.*, lecithins (in egg yolk, brain)	Glycerol, $C_3H_5(OH)_3$	Phosphoric, H_3PO_4 Oleic, $C_{17}H_{33}COOH$ Palmitic, $C_{15}H_{31}COOH$ Choline, $(CH_3)_3N(OH)C_2H_4OH$
2. Glycolipides, *e.g.*, kerasin (in brain)	Galactose, $C_6H_{12}O_6$	Lignoceric, $C_{23}H_{47}COOH$ Sphingosine, $C_{18}H_{33}(OH)_2NH_2$
III. Derived lipides:		
1. Fatty acids (in fats)		Oleic, $C_{17}H_{33}COOH$
2. Sterols (in fats, waxes)	Cholesterol, $C_{27}H_{45}OH$	

* For a given fat, *e.g.*, butter, the typical rather than the total products of hydrolysis are listed. Fatty acids, wax alcohols, and sterols may occur free or combined. They are also classed as derived lipides.

available that acts on the ester to be hydrolyzed, or by means of strong acids or superheated steam. A more convenient and widely used method consists in subjecting the ester to the action of a strong alkali such as sodium hydroxide, whereby the alcohol and a salt of the acid are produced:

$$\underset{\text{Butyl acetate}}{C_4H_9O\overset{\overset{O}{\|}}{C}CH_3} + \underset{\text{Sodium hydroxide}}{NaOH} \longrightarrow \underset{\text{Butyl alcohol}}{C_4H_9OH} + \underset{\text{Sodium acetate}}{NaO\overset{\overset{O}{\|}}{C}CH_3}$$

This process is called saponification. If it is desired to obtain the organic acid itself, the solution of the sodium salt may be treated with a strong mineral acid:

$$\underset{\text{Sodium acetate}}{NaOCCH_3} + \underset{\text{Sulfuric acid}}{H_2SO_4} \longrightarrow \underset{\text{Sodium acid sulfate}}{NaHSO_4} + \underset{\text{Acetic acid}}{HOCCH_3}$$

TRUE FATS

Definition

The true fats may be defined as esters of the trihydroxy alcohol, glycerol, and the higher fatty acids. The esters of glycerol are called glycerides, a natural fat being a mixture of various glycerides in different proportions. The terms *fat* and *oil* are used to distinguish between solid and liquid fats. If the substance is solid at 20°C., it is spoken of as a fat. If it is a liquid at this temperature, it is regarded as an oil. The use of the term oil in this connection must not be confused with its use as applied to so-called mineral oils, such as kerosene oil which is a hydrocarbon, and not related to fats.

Occurrence and importance

The fats are abundant in both plant and animal materials such as cottonseed, peanut, coconut, olive, milk, butter, cheese, and meats. The cereals as a rule are comparatively low in fat, since starch takes the

Table 4–2

Economic importance of some industries based on fats *

Industry	*Wage earners*	*Value of products shipped*
1. Oils (vegetable and animal)	30,959	$1,741,238,000
2. Butter	30,131 †	1,037,000,000
3. Soap and glycerine	27,660	1,085,789,000
4. Grease and tallow	12,472	304,535,000
5. Shortenings (vegetable)	8,003	884,713,000
6. Oleomargarine	2,567	214,598,000
	111,792	$5,267,873,000

* Compiled from the 1947 *Census of Manufactures*, Bureau of the Census, 1950, and from the *Statistical Abstract of the United States, 1951*, published by the Department of Commerce.

† Estimated in part.

place of fat in the composition of such seeds. It is noteworthy that the seeds of the tropical regions of the earth are generally characterized by

a high fat content, while those of the temperate zone are usually high in starch. This is only a general rule since there are many exceptions; rice, which is a tropical product, contains little fat, and soybean, which contains much fat, grows in temperate regions. The fats of commerce are removed from the material in which they occur either by mechanical means or by extraction with suitable solvents. The mechanical methods are more generally used. They may vary widely—churning in the making of butter, heating and filtering in the rendering of lard and tallow, pressing, with or without the aid of heat, in obtaining olive, cottonseed, and other oils.

Elementary composition

The fats are comparatively high in carbon and low in oxygen. This is in sharp contrast to the carbohydrates, which contain a high percentage of oxygen. A comparison of the elementary composition of fat, starch, and protein is as follows:

per cent:	*Carbon*	*Hydrogen*	*Oxygen*	*Nitrogen*	*Physiological fuel value Calories per gram*
Fat	76.5	12.0	11.5	—	9.0
Starch	44.4	6.2	49.4	—	4.0
Protein	53	7	23	16	4.0

From the above table it is evident that fats have a considerably higher heat value than either proteins or carbohydrates. On oxidation in the body, fats give two and one-fourth times as much heat as the other foodstuffs. This is because of the higher content of carbon and hydrogen in fats.

Lipides such as lecithin and cephalin, closely related to the true fats, contain, in addition, the elements phosphorus and nitrogen. As a class, however, lipides (and carbohydrates) do not contain nitrogen and thus are sharply differentiated from proteins.

Products on hydrolysis

Some idea regarding the nature of a fat may be obtained by breaking down the fat into its constituent parts—that is, by hydrolyzing it. Whenever a natural fat is hydrolyzed by acids or enzymes, glycerol and a number of fatty acids are obtained. The fatty acids are divided into two series, the saturated and the unsaturated. A study of these acids is indispensable to a proper understanding of the fats themselves.

Glycerol, $C_3H_5(OH)_3$

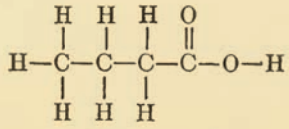
During and after World War I, considerable quantities of glycerol, or glycerine as it is commonly called, were produced by a yeast fermentation process. Today, however, it is obtained mainly as a by-product of the soap industry. The liquors that remain after the soap has been removed are distilled in a vacuum, and by a series of fractionations glycerol is obtained free from impurities. In many cases the glycerol is not removed from the soap. If left in, it tends to make the soap transparent and of better quality. A process for the manufacture of glycerol from certain petroleum fractions has also been developed.

Glycerol is a viscous, colorless liquid that has a sweet taste and no odor. It is extensively used in the manufacture of nitroglycerine, an ester of glycerol and nitric acid, $C_3H_5(NO_3)_3$, which is the basis for a large number of explosives such as dynamite, blasting gelatin, etc. Nitroglycerine also finds use as a drug for alleviation of the severe pain associated with some types of heart disease. Glycerol is also widely used as a solvent in many technical operations. It is extensively used in the manufacture of cosmetics and toilet and pharmaceutical preparations. It can be used both internally and externally with perfect safety and, in fact, can be utilized as a food by human beings.

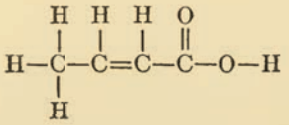
The saturated fatty acids

Saturated fatty acids contain all the hydrogen with which they are capable of uniting, whereas unsaturated fatty acids contain carbon atoms joined together by double bonds and hence can unite with more hydrogen.

Thus it may be seen from the following graphic formulas that butyric acid is saturated and crotonic acid is unsaturated:



Butyric acid



Crotonic acid

Saturated acids have a higher melting point than unsaturated fatty acids with the same number of carbon atoms. Hard fats, such as tallow, give a high percentage of saturated acids, and soft fats, a low percentage.

Since natural fats are mixtures of various glycerides, a large number of fatty acids is obtained on hydrolysis. The following table gives the principal fatty acids of the saturated series:

Table 4–3

Saturated fatty acids

Name	*Formula* ($C_nH_{2n+1}COOH$)	*Typical Occurrence*
Formic	$HCOOH$	Not in fats
Acetic	CH_3COOH	Not in fats
Propionic	CH_3CH_2COOH	Not in fats
Butyric	$CH_3(CH_2)_2COOH$	Butter
Caproic	$CH_3(CH_2)_4COOH$	Butter, coconut and palm oils
Caprylic	$CH_3(CH_2)_6COOH$	Coconut and palm oils, butter
Capric	$CH_3(CH_2)_8COOH$	Coconut and palm oils, butter
Lauric	$CH_3(CH_2)_{10}COOH$	Laurel, coconut and palm oils
Myristic	$CH_3(CH_2)_{12}COOH$	Butter, wool fat, spermaceti
Palmitic *	$CH_3(CH_2)_{14}COOH$	All animal and vegetable fats, notably lard
Stearic *	$CH_3(CH_2)_{16}COOH$	Animal and vegetable fats, notably tallow
Arachidic	$CH_3(CH_2)_{18}COOH$	Peanut oil

* Most abundant fatty acids. See Table 4–5.

An examination of the table shows that only fatty acids containing an even number of carbon atoms are obtained from natural fats. Although there are several important exceptions to this statement, it is nevertheless true for the great majority of fats. This rule is rather suggestive of the way in which the fats must be built up in nature. It is probable that fatty acids are formed in nature by addition of units containing two carbon atoms, giving rise only to acids with an even number of carbon atoms. The saturated acid obtained in greatest amount from fats is palmitic. Stearic acid is also obtained in large quantities but not to the same extent as palmitic. The fatty acids, such as butyric, of lower molecular weight are found to a considerable extent as glycerides in butter and coconut oil, but except in these two fats they occur in comparatively small amounts. Some of the lower fatty acids such as formic, acetic, and propionic acid belong to the series of saturated fatty acids, but no glycerides of these acids are found in natural fats. Small amounts of these acids, and other fatty acids of low molecular weight, are found free in perspiration and urine. Salts and esters of fatty acids of both low and high molecular weight are contained in the feces.

Butyric acid is a colorless, mobile liquid boiling at 162°C. and is completely miscible with water. Caproic and caprylic acids are also liquids at room temperatures; capric acid is a semisolid, but lauric acid is definitely a solid. The change from liquid to solid is thus associated with