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## Review of Excipients and pH's for Parenteral Products Used in the United States

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**ABSTRACT:** *Excipients used in U.S. parenteral products were categorized according to their function. The concentrations used in commercial products were also identified. The range of pH value in various products was tabulated with emphasis on products with extreme pH's. The uses of excipients in parenteral dosage form were discussed.*

### Introduction

The choice of excipients used in parenteral products is not as liberal as in other dosage forms because of two major concerns: safety in parenteral use and feasibility in sterilization. Acceptance of a substance to be used as an excipient in parenteral products often involves lengthy safety testing or production trials. To avoid uncertainty, most formulators tend to employ compounds used in existing parenteral products. This survey is intended to provide an overall view of excipients used in parenteral products available in the United States. For reason of stability or solubility the pH of a product could not always be adjusted to physiological pH (7.4). When problems arise formulators are often inquisitive about the pH of other products. This review, therefore, focuses on products with extreme pH's, and shows tabulation of pH range, acid or base used for adjustment, and product identity.

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### Method

The *Physician's Desk Reference* (PDR), 1977-1980 editions (1), were the major source of information. For products not described in the PDR, manufacturers were contacted and the package inserts solicited.

Excipients were categorized according to their presumed function in the formulation. Concentrations were all calculated on % (w/v) base. For dry products, concentrations were calculated according to the commonly diluted volume. For each excipient, ascending concentrations were illustrated by the corresponding products and manufacturer. Examples of only three products were given if there were three or more products containing the same concentration of excipient. One exception is the category of buffer for which only the highest concentration was listed. All of this is shown in Table I.

Many products did not list pH in the PDR. Nevertheless, in these cases information was gathered from other references (2, 3), and Table II illustrates the variety of products employing extreme pH's. For conciseness only one example was given for each particular pH range.

### Discussion

This survey brought to light the use of a few excipients uncommon for parenteral use such as phenylmercuric nitrate, dioctyl sodium sulfosuccinate, pectin, etc. Most of these excipients were found in old formulations not covered by the present FDA regulations. On the other hand, some excipients recommended

TABLE I. Excipients for Parenteral Products

*I. Antimicrobial Preservatives*

1) Benzyl alcohol	0.5%	Cleocin Phosphate (Upjohn)
	0.75%	Stelazine (SKF)
		Compazine (SKF)
	0.83%	Solu-Medrol (Upjohn)
	0.88%	Cortisone Acetate (Upjohn)
	0.9%	Pronestyl (Squibb)
		Kenolog (Squibb)
		Vistaril (Pfizer)
	1.0%	Solu-Medrol (Upjohn)
	1.2%	Prolixin Decanoate (Squibb)
	1.5%	Valium (Roche)
		Vesprin (Squibb)
	2.0%	Adrenosem (Beecham)
		Aminophyllin (Searle)
4.0%	Kestrin (Hyrex)	
5.0%	Durabolin (Organon)	
10.0%	Deca-Durabolin (Organon)	
2) Benzethonium chloride	0.01%	Ketaject (Bristol)
		Flexoject (Mayrand)
3) Butylparaben	0.015%	Duracillin A.S. (Lilly)
4) Chlorobutanol	0.25%	Nydrazid (Squibb)
		Novocain (Winthrop)
	0.5%	Hexa-Betalin (Lilly)
5) Metacresol		Atropine Sulfate (Lilly)
	0.16%	NPH Iletin (Lilly)
	0.1%	Demerol Hydrochloride (Winthrop)
	0.25%	Protamine, Zinc & Iletin (Lilly)
6) Methylparaben	0.01%	Lidoject-1 (Mayrand)
	0.045%	Celbenin (Beecham)
	0.065%	Apresoline Hydrochloride (Ciba)
	0.1%	Bicillin L-A (Wyeth)
		Prolixin (Squibb)
		Talwin (Winthrop)
	0.13%	Crysticillin (Squibb)
	0.15%	Neo-Betalin 12 (Lilly)
	0.18%	Garamycin (Schering)
		Bactocill (Beecham)
7) Myristylgamma picolinium chloride	0.17%	Depo-Provera (Upjohn)
8) Phenol	0.065%	NPH Iletin (Lilly)
	0.18%	Crysticillin (Squibb)
	0.25%	Ergotrate Maleate (Lilly)
	0.45%	Tensilon (Roche)
		Prostigmin (Roche)
	0.5%	Sus-Phrine (Berlex)
		Tagamet (SKF)

*continued*

TABLE I. *Continued*

9) Phenylmercuric nitrate	0.001%	Estradurin (Ayerst)
10) Propylparaben	0.005%	Bactocill (Beecham)
		Celbenin (Beecham)
	0.01%	Prolixin (Squibb)
		Bicillin L-A (Wyeth)
		Bicillin C-R (Wyeth)
	0.02%	Crysticillin (Squibb)
		Garamycin (Schering)
	0.035%	Apresoline Hydrochloride (Ciba)
11) Thimerosal	0.001%	Wydase (Wyeth)
	0.01%	Test-Estrin (Marlyn)
		MICRhoGAM (Ortho)
	0.02%	Theelin R-P (Parke-Davis)
<i>II. Solubilizers, Wetting Agents or Emulsifiers</i>		
1) Dimethylacetamide	0.01%	Serpasil (Ciba)
2) Dioctyl sodium sulfosuccinate	0.015%	Testoject (Mayrand)
3) Egg yolk phospholipid	1.2%	Intralipid 10% (Cutter)
4) Ethyl alcohol	0.61%	Syntocinon (Sandoz)
	3.0%	Morrhuate Sodium (Lilly)
	6.0%	Kestrin (Hyrex)
	10.0%	Valium (Roche)
		Dilantin (Parke-Davis)
	49.0%	Crystodigin (Lilly)
5) Ethyl lactate	0.1%	Ergotrate Malcate (Lilly)
6) Glycerin	14.6%	Gynergen (Sandoz)
	15.0%	Cedilanid-D (Sandoz)
		DHE 45 (Sandoz)
	25.0%	Sus-Phrine (Berlex)
7) Lecithin	0.5%	Bicillin L-A (Wyeth)
		Wycillin (Wyeth)
	1.5%	Duracillin A.S. (Lilly)
	2.3%	Crysticillin (Squibb)
8) PEG-40 Castor oil <sup>a</sup>	7.0%	AquaMEPHYTON (MSD)
	11.5%	Monistat (Janssen)
9) Polyethylene glycol 300	0.01%	Apresoline Hydrochloride (Ciba)
	5.0%	Serpasil (Ciba)
	30.0%	Sandril (Lilly)
	50.0%	Seconal sodium (Lilly)
		Robaxin (Robins)
10) Polysorbate 20	0.01%	Test-Estrin (Marlyn)
11) Polysorbate 40	0.05%	Bicillin L-A (Wyeth)
12) Polysorbate 80	0.04%	Kenalog (Squibb)
	0.18%	Depo-Provera (Upjohn)
	0.20%	Aristospan (Lederle)
	0.39%	Cortisone Acetate (Upjohn)

*continued*

TABLE I. *Continued*

	0.40%	Aristospan (Lederle)
		Duracillin A.S. (Lilly)
13) Povidone	4.0%	Librium (Roche)
	0.2%	Kestrin (Hyrex)
	0.3%	Crysticillin (Squibb)
		Wycillin (Wyeth)
	0.5%	Crysticillin (Squibb)
	0.55%	Bicillin C-R (Wyeth)
14) Propylene glycol	0.6%	Bicillin L-A (Wyeth)
	1.0%	Duracillin A.S. (Lilly)
	0.2%	Estradurin (Ayerst)
	20.0%	Librium (Roche)
	40.0%	Valium (Roche)
		Dilantin (Parke-Davis)
	50.0%	Dramamine (Searle)
15) Sodium desoxycholate		Dramoject (Mayrand)
16) Sorbitan monopalmitate	0.21%	Fungizone (Squibb)
17) Theophylline	0.05%	Bicillin L-A (Wyeth)
	5.0%	Dicurin Procaine (Lilly)
<i>III. Buffers</i>		
1) Acetic acid	0.22%	Neo-betalin 12 Crystalline (Lilly)
2) Adipic acid	1.0%	Serpasil (Ciba)
3) Benzoic acid and sodium benzoate	5.0%	Valium (Roche)
4) Citric acid	0.5%	Aldomet (MSD)
5) Maleic acid	1.6%	Librium (Roche)
6) Potassium phosphate	0.1%	Ouabain (Lilly)
7) Sodium phosphate monobasic	1.7%	Solu-Medrol (Upjohn)
8) Sodium phosphate dibasic	0.71%	Celestone (Schering)
9) Lactic acid	0.1%	Ergotrate Maleate (Lilly)
10) Sodium acetate	0.8%	Soluject (Mayrand)
11) Sodium bicarbonate	0.005%	Amipaque (Winthrop)
12) Sodium carbonate	0.06%	Brevital (Lilly)
13) Sodium citrate	4.0%	Duracillin A.S. (Lilly)
14) Sodium tartrate	1.2%	Compazine (SKF)
15) Tartaric acid	0.65%	Priscoline (Ciba)
<i>IV. Antioxidants</i>		
1) Acetone sodium bisulfite	0.2%	Talwin (Winthrop)
		Bronkheprine (Breon)
	0.4%	Novocain (Winthrop)
	0.8%	Novocain (Breon)
	0.05%	Serpasil (Ciba)
	0.1%	Torecan (Boehringer)
	0.2%	Thorazine (SKF)
2) Ascorbic acid	1.0%	Sus-phrine (Cooper)
		Sandril (Lilly)
	3.0%	Tetracyc IV (Pfizer)

*continued*

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