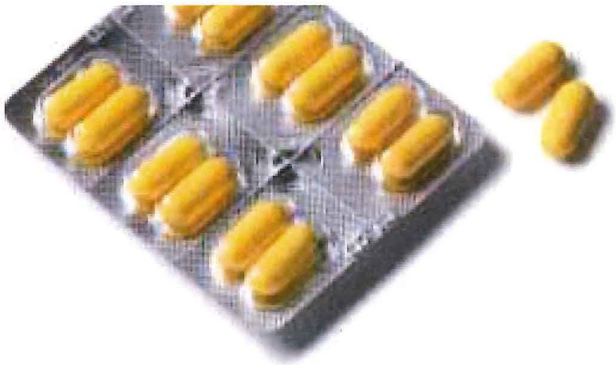
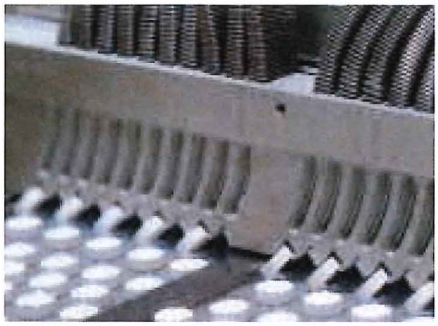
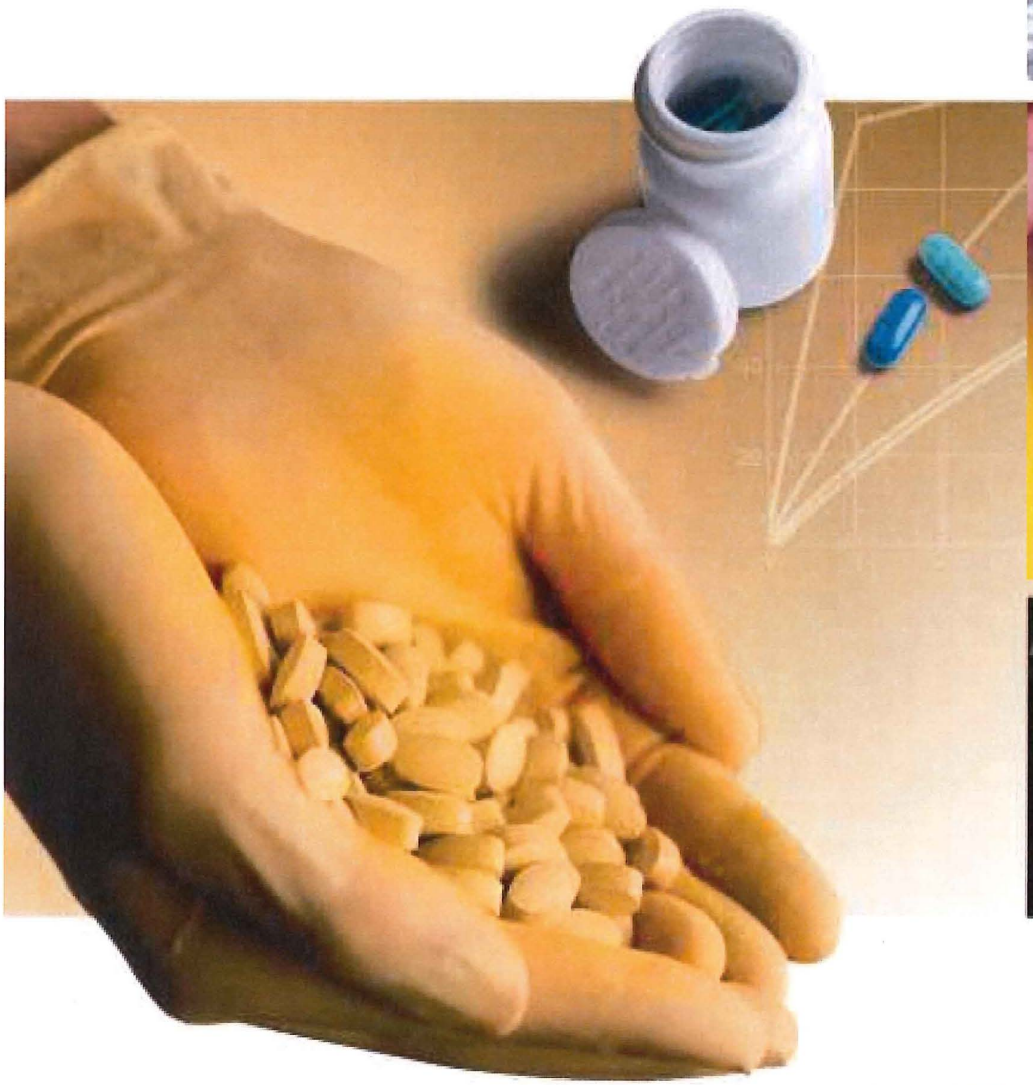


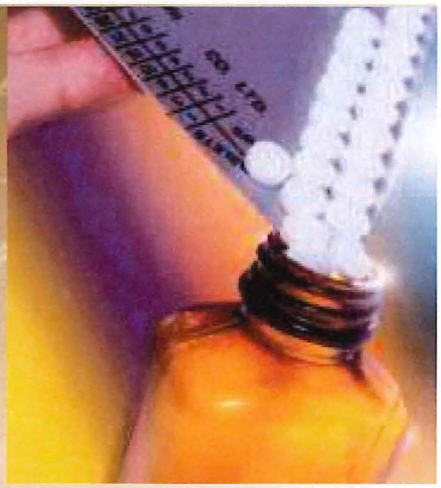
DOW

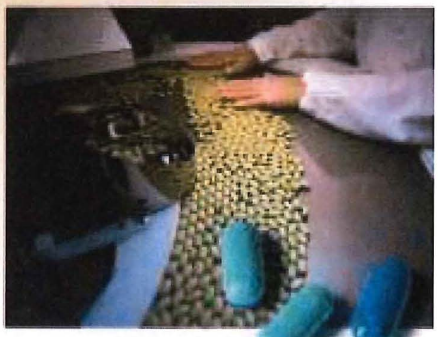
POLYOX Water-Soluble Resins NF

in Pharmaceutical Applications









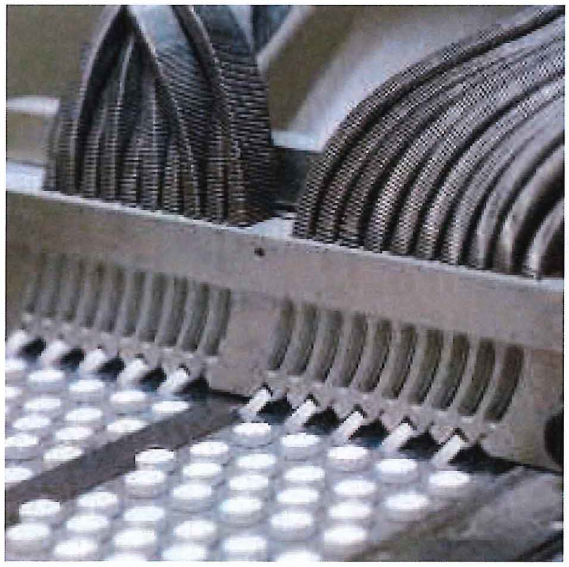
An Introduction to POLYOX Water-Soluble Resins

POLYOX™ Water-Soluble Resins, NF Grade are nonionic poly (ethylene oxide) polymers that meet all the specifications of the *United States Pharmacopoeia—National Formulary.* They are white, free-flowing hydrophilic powders supplied in a wide variety of molecular weight grades, ranging from one hundred thousand to seven million daltons or amu.

They are essentially tasteless, colorless, nonionic, and non-caloric. This unusual combination of properties makes them useful in a surprisingly broad array of pharmaceutical formulations. They have a long history of successful applications in uses such as controlled release solid dose matrix systems, transdermal drug delivery systems, and mucosal bioadhesives.

Extremely Fast Hydration and Gel Formation

POLYOX Resins are among the fastest-hydrating water-soluble polymers used in pharmaceutical systems. They very quickly form hydrogels that initiate and regulate release of active ingredients. Systems using POLYOX Resins are often superior to others in approaching zero order release models.



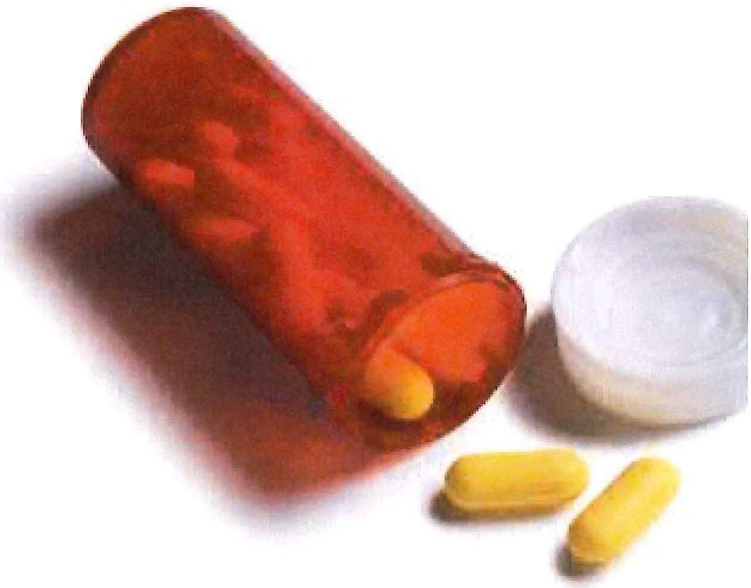
Unusually Wide Range of Molecular Weights

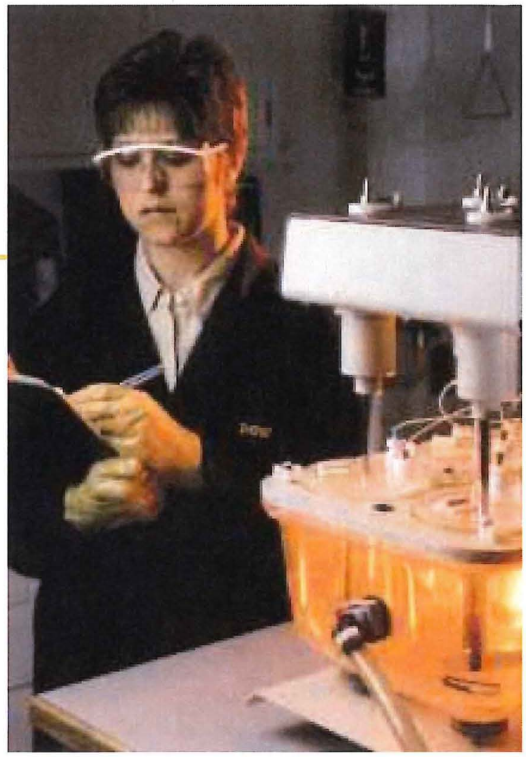
With molecular weights ranging from 100,000 to 7,000,000, POLYOX Water-Soluble Resins offer exceptional formulating latitude. You can select from many different options to help control dosage size, matrix release profiles, and production methods while maintaining consistent flow properties and tablet performance.

Compliance With FDA and Other Regulatory Requirements

POLYOX Water-Soluble Resins, NF Grade comply with the USP polyethylene oxide NF monograph.

These products meet the requirements of the Food Chemicals Codex, the International Codex Alimentarius, and the U.S. National Formulary (NF). These products have also been approved in drug products sold in all major European countries. Approval for use in Japan is under way and anticipated. The NF product family is listed in Table 1.





More Technical Assets to Help You Succeed Quickly

With an expanded technical staff and assets of The Dow Chemical Company, we can offer an unusually broad and synergistic body of excipient knowledge. Our strong team of technical individuals in several global locations is actively engaged in product development, technology development, and pharmaceutical applications support. So when you need help with technical issues involving excipient behavior, product selection, and formulation optimization, we can respond in surprisingly powerful ways.

Table 1 — POLYOX Water-Soluble Resins For Pharmaceutical Applications

POLYOX Water-Soluble Resins, NF Grade	Approximate Molecular Weight	Viscosity Range at 25°C, cP			Brookfield Viscometer, Model RVF, Spindle No./Speed, rpm
		5% Solution	2% Solution	1% Solution	
WSR N-10 NF	100,000	30 – 50			1/50[1]
WSR N-80 NF	200,000	55 – 90			1/50[1]
WSR N-750 NF	300,000	600 – 1,200			1/10
WSR-205 NF	600,000	4,500 – 8,800			2/2
WSR-1105 NF	900,000	8,800 – 17,600			2/2
WSR N-12K NF	1,000,000		400 – 800		1/10
WSR N-60K NF	2,000,000		2,000 – 4,000		3/10
WSR-301 NF	4,000,000			1,650 – 5,500	2/2
WSR Coagulant NF	5,000,000			5,500 – 7,500	2/2
WSR-303 NF	7,000,000			7,500 – 10,000	2/2

The physical property data listed are considered to be typical properties, not specifications.

[1]Model RVT.

An Ideal Choice for Controlled Release Systems

A hydrophilic matrix tablet is a simple-to-formulate, yet effective sustained-release drug-delivery system in which a bio-active is uniformly distributed within a polymer matrix. The drug release mechanism is controlled by several variables in a dynamic process. Upon wetting of the tablet, the polymer on the tablet surface hydrates to form a gel layer. The drug diffuses from this surface gel layer, which expands with time into the interior of the tablet, allowing diffusion of the drug from the tablet core.

POLYOX Water-Soluble Resins are very hydrophilic polymers. They hydrate rapidly to form a gel layer on the tablet surface for the release of actives. Because POLYOX Resins are non-ionic, no interaction between drug and polymers is to be expected. The data presented here show how molecular weight and concentration of POLYOX Resins affect the release rate of a model water-soluble and water-insoluble drug in a matrix system.

Experimental Procedure

Tablet formulations (Table 2) were dry-blended in a double planetary mixer. Tablets were pressed with a single punch Carver Laboratory Press in a one-half inch diameter die with a compression force of one metric ton. Drug release data were obtained from uncoated tablets in a USP-specified dissolution apparatus, which was equipped with baskets. The dissolution medium was simulated gastric fluid (without pepsin) at 37°C. Rotation speed of the baskets was kept at 50 rpm. All data presented here represent an average of a minimum of three determinations. UV/visible spectroscopy was used to determine the concentration of the actives in the dissolution media.

Results

Molecular Weight

Figure 1 shows the effect of molecular weights of POLYOX Water-Soluble Resins on the release rate. Increasing the molecular weight while maintaining a constant polymer concentration can drastically reduce the release rates. The increased molecular weight leads to an increase in gel strength, which tends to decrease the diffusion of the drug; however, there is a maximum molecular weight beyond which no further change in release rate is affected. As can be seen, an increase in molecular weight from 5,000,000 to 7,000,000 does not appreciably alter the release rate for the water-soluble active, caffeine.

Figure 1 — Effect of Molecular Weight of POLYOX Water-Soluble Resins on *In Vitro* Release Rate of Caffeine From a Matrix Tablet

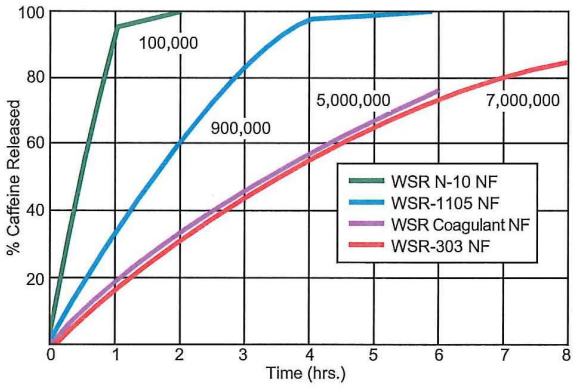


Table 2 — Tablet Formulations

Weight Percent, Based on 500-mg Tablet

Ingredients	A	B	C	D	E	F	G
Caffeine	10	20	30	20	20	–	–
Riboflavin	–	–	–	–	–	5	20
POLYOX Water-Soluble Resin NF	20	20	20	10	60	10	20
Lactose	69	59	49	69	19	84	59
Magnesium Stearate	1	1	1	1	1	1	1

Polymer Concentration

Figure 2 illustrates the effect of polymer concentration on release rate. Increasing polymer concentration increases the gel viscosity on the surface of the tablets, which will retard the diffusion of the drug from the gel layer. Increasing the concentration from 20 to 60 percent of a relatively low molecular weight POLYOX Water-Soluble Resin results in a drug release profile very similar to that obtained from 20 percent of a high molecular weight POLYOX Resin. However, this concentration effect is seen only for low molecular weight polymer. Figure 3 shows caffeine release from matrix tablets produced from POLYOX WSR-303 NF (7,000,000 molecular weight). When polymer concentration was changed from 10 to 60 percent in the formulation, no drastic changes in the release rate was observed. At a very low polymer concentration, the initial drug release is larger, but the rate of release is very similar to that obtained for higher polymer concentrations.

Figure 2 — Effect of Polymer Concentration and Molecular Weight on *In Vitro* Release Rate of Caffeine From a Matrix Tablet With POLYOX WSR-1105 NF

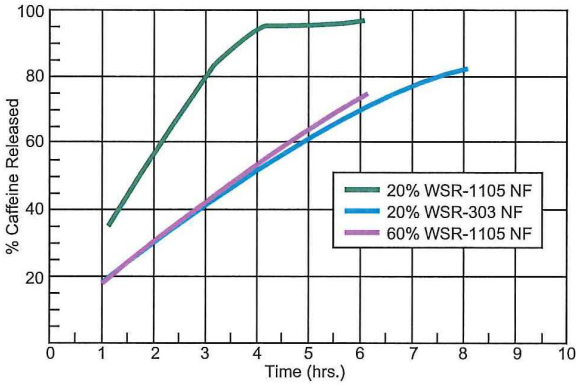
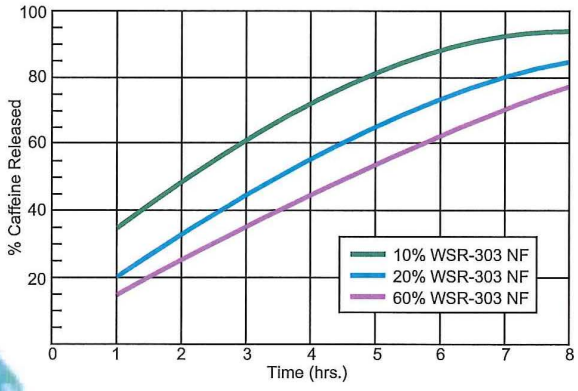
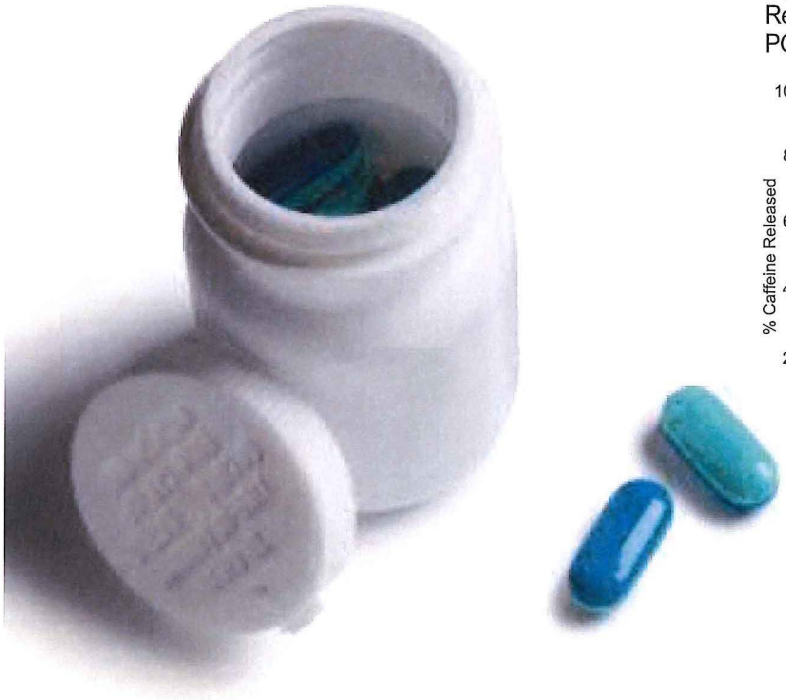


Figure 3 — Effect of Polymer Concentration on *In Vitro* Release Rate of Caffeine From a Matrix Tablet With POLYOX WSR-303 NF





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