CHAPTER I

INTRODUCTION

Solid drugs administered orally for systemic activity must dissolve in the gastrointestinal fluids prior to their absorption. Thus, the dissolution rate of drugs in gastrointestinal fluids could influence the rate and extent of their absorption. Inasmuch as the rate of dissolution of a solid is a function of its solubility in the dissolution medium, the latter could influence the absorption of relatively insoluble drugs. Drugs with poor solubility are absorbed with difficultly, and the rate of dissolution of such compounds in gastrointestinal fluids is generally the rate controlling step for absorption (1). To ensure the bioavailability of a poorly soluble drug, USP XXI & NF XVI (2), requires almost 400 preparations to be tested for dissolution.

Solid dispersion has been used to improve the dissolution of poorly soluble drugs. In solid dispersion systems an insoluble drug is dispersed with an inert soluble solid matrix. The dispersion of a drug within a water-soluble carrier effectively cause a reduction in particle size of the dispersed drug. Upon exposure to the dissolution medium, the carrier dissolves rapidly and the finely dispersed particles are released with optimum properties for dissolution.

Solid dispersions can be obtained by three main procedures: by melting (fusion) method, by solvent (coprecipitation) method, and by melting-solvent method. Single and combined water-soluble carriers have been used as carrier systems for solid dispersions. The combined water-soluble carrier system was reported to be better carrier system for solid dispersions than the single water-soluble carrier system (3).

Prednisolone and indomethacin showed low solubilities in water (4). Prednisolone has been included in a list of substances susceptible to biological problems (5). Indomethacin absorption was reported to be formulation dependence and the drug has been classified under demonstrating clinical inequivalence among its formulation (6). The USP XXI & NF XVI (2) requires minimum dissolution rates for both prednisolone tablets and indomethacin capsules.

In the present study solid dispersion was applied to enhance the dissolution rates of these poorly water-soluble drugs. Coprecipitation technique was chosen to prepare solid dispersions in this study because prednisolone decomposes to some degree at its melting points (7) and dextrose also decomposes at high temperature, manifested by an amber discoloration.

Single and combined water-soluble carriers were utilized. System of dextrose-polyethylene glycol 4000 (PEG 4000), dextrose-sodium lauryl sulfate (SLS) were used as combined water-soluble carriers for prednisolone and indomethacin coprecipitates. Dextrose, PEG 4000, and SLS were also used as single carriers for both drugs.

PEG 4000, dextrose, and some surfactants are inert water-soluble carriers which have been employed in preparing solid dispersions of many poorly water-soluble drugs. A surfactant, SLS, was selected because it also act as a lubricant in tablet formulation, the same as PEG 4000. Dextrose has long been utilized for tablet preparation and it is nontoxic, inexpensive, and physiologically acceptable.

The objectives of the investigation were to:

1. Formulate prednisolone tablets and indomethacin tablets from drug-single carrier coprecipitates (drug-dextrose, drug-PEG 4000, drug-SLS), drug-combined carrier coprecipitates (drug-dextrose-PEG 4000, drug-dextrose-SLS), drug-single carrier mixtures (drug-dextrose, drug-PEG 4000, drug-SLS), drug-combined carrier mixtures (drug-dextrose -PEG 4000, drug-dextrose-SLS).

2. Compare the disintegration times of tablets prepared from coprecipitates with tablets prepared from mixtures.

3. Compare the dissolution rate of drug from tablets containing drug-carrier(s) coprecipitates and drug-carrier(s) physical mixtures.

4. Study the effect of the amount of carriers on the dissolution rate of drug from these tablets.

5. Study the effect of types of carriers on the dissolution of these tablets.

6. Evaluate the influence of the combined water-soluble carriers and the single water-soluble carriers on the dissolution rates of prednisolone and indomethacin tablets.

Literature Review

1. Historical Background

A number of modern therapeutic agents are poorly soluble in the aqueous fluids of gastrointestinal tract. Consequently, the in-vivo dissolution rate of these compounds is low and their gastrointestinal absorption tends to be incomplete and erratic. Since dissolution rate is directly proportional to the surface area, one may increase the rate by decreasing particle size of the drug. The greater the surface area, rapid the dissolution and thereby, faster absorption, provided that the absorption is rate limited by the dissolution process.

In 1961, Sekiguchi and Obi (8), became the first to propose the use of solid dispersions to increase dissolution and oral absorption of poorly water-soluble drugs. They investigated the formation of a eutectic mixture between the drug and a physiologically inert water-soluble carrier. The physical mixture of drug and carrier was heated, and the drug was dissolved in the melted carrier. They found that the cooled sample contained finely dispersed drug particles in the carrier matrix.

Goldberg et al. (9) suggested the use of solid solutions in order to reduce the particle size of drugs. This technique, now called the melt method, essentially involves dissolving the drug in a melted carrier and flash-cooling the liquid (or melt) to form a homogeneous dispersion. Tachibana and Nakamura (10) reported a

novel method for preparing aqueous colloidal dispersions of β-carotene by using water-soluble polymers such as polyvinylpyrrolidone. They dissolved the drug and the polymer carrier in a common solvent and then evaporated the solvent completely. A colloidal dispersion was obtained when the coprecipitate was exposed to water.

Chiou and Riegelman (11) advocated the application of glass solution to increase dissolution rates. This glassy state, or glass solution, exhibited very rapid dissolution rates with many drugs such as griseofulvin (12) and sulfabenzamide (13).

It was proposed that the enhancement of dissolution and absorption rate of various drugs dispersed in a carrier was primarily due to the molecular and colloidal dispersion of the drug in the highly water soluble carrier (11,12,14).

To date two solid dispersion systems, Gris-PEG (Sandoz-Wander) a griseofulvin-polyethylene glycol solid dispersion and Cesamet (Lilly) a nabilone-polyvinylpyrrolidone solid dispersion, are known to have reached the market place.

2. Definition of Solid Dispersions

The most widely used definition of solid dispersions is that put forward by Chiou and Riegelman in 1971 (12). The term refers to the dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by melting, solvent, or melting-solvent method.

Depending on whether the matrix is water soluble, the drug's dissolution can be decreased or enhanced. A water-soluble carrier results in a fast release of the drug from the matrix, and a poorly soluble or insoluble carrier leads to a slower release of the drug from the matrix. To achieve a fast release of a drug from the matrix, it is generally necessary that the active drug be minor component in the dispersion system in terms of the percent weight.

3. Methods of Preparation

Solid dispersions can be obtained by three main procedures:

3.1 By melting method (fusion technique)

3.2 By solvent method (coprecipitation technique)

3.3 By melting-solvent method

3.1 Melting or Fusion Method

In this method, the physical mixture of a drug and a water-soluble carrier was heated directly until it melted. The melt mixture was then cooled and solidified rapidly in an ice bath under vigorous stirring. The final solid mass was crushed, pulverized, and sieved.

Before a solid dispersion can be prepared by the melting method, the drug must chemically stable in the melted carrier. Color changes in the melt or shifts in the ultraviolet spectrum generally indicate instability. Differential thermal analysis (DTA) and thin layer chromatography are useful tools to test for drug stability. The drug must also dissolve in the molten carrier if the melting method is to be successful (15).

The melting method has been employed to improve dissolution rates of many poorly soluble drugs such as griseofulvin (11), diazepam (16), digitoxin (17), tolbutamide (18), dicumarol (19), and prednisone (20).

For the melting method polyethylene glycol of 4000, 6000, and 20000 molecular weights have been employed extensively as inert water-soluble carriers.

3.2 Solvent or Coprecipitation Method

This method entails the dissolution of a physical mixture of drug and carrier in a common solvent, followed by evaporation of the solvent and resultant coprecipitation of drug and carrier.

The solvent system used in the preparation of dispersions is exceedingly important. The ingredients of the dispersion should be very soluble in the solvent, or crystallization of one may take place before the other and a uniform dispersion will be derived (15).

Polyvinylpyrrolidone (or povidone) has been a popular choice as an inert carrier for dispersions prepared by solvent method. Among several examples, griseofulvin (21), sulfathiazole (22), reserpine(23), digoxin(24) demonstrated faster dissolution rates when they were dispersed in polyvinylpyrrolidone (PVP) by the solvent method.

Due to chemical stability to heat, solid dispersions with

PVP and deoxycholic acid can only be prepared by the solvent method, since both materials have melting points above 170 °C (15).

PEG 4000, PEG 6000, and PEG 20000 also have been utilized as carriers for coprecipitation of some poorly soluble drugs such as diazepam (16), chlorothiazide (25), tolbutamide (3), and griseofulvin (11).

3.3 Melting-solvent Method

Chiou and Smith (26) formed solid dispersions by dissolving the solid active ingredients in a solvent and subsequently incorporating the solution into a molten carrier. The mixture was then solidified. In cases where the active constituent was a liquid, the liquid was simply mixed with the molten carrier and solidified by cooling (12).

4. Comparison between the Methods of Preparing Solid Dispersions

Elworthy and Lipscomb (27) found that the release rate of tolbutamide from solid dispersions in polyethylene glycol 4000 or 6000 was greater from coprecipitated dispersions than from fused dispersions.

McGinity et al. (16) prepared melt and coprecipitates of sulfabenzamide. A comparison of the dissolution rates indicated that coprecipitation technique was superior than the melting technique in the cases of sulfabenzamide-mannitol and sulfabenzamide-PEG 6000 solid dispersions, but fusion technique was superior in the cases of sulfabenzamide-urea and sulfabenzamide-dextrose solid dispersions.

Anastasiadou et al. (16) demonstrated that solid dispersions of diazepam in PEG 4000 prepared by coprecipitation method produced more diazepam dissolution rate enhancement than the solid dispersions prepared by fusion method.

The nalidixic acid-hexamine and nalidixic acid-Myrj 59 coprecipitates were found to yield more nalidixic acid dissolution improvement than the nalidixic acid-hexamine and nalidixic acid-Myrj 59 prepared by fusion method (28). However, nalidixic acid-urea coprecipitates showed less dissolution rate enhancement comparing to the nalidixic acid-urea fusion system (29).

Suvanakoot (30) showed that coprecipitation technique was superior to fusion technique in term of dissolution rate enhancement of phenylbutazone and tolbutamide using PEG 20000 as the inert carrier.

From these studies coprecipitation technique, in most cases, appeared to yield better dissolution rate improvement of poorly water soluble drugs than the fusion technique. Besides, by using solvent method thermal decomposition of drugs or carriers could be prevented because of the low temperature required for the evaporation of organic solvents.

5. Coprecipitation Technique

Coprecipitate can be prepared by three procedures:

5.1 Simple evaporation

5.2 Lyophilization

5.3 Spray drying

5.1 Simple Evaporation

By this procedure the solution containing drug and carrier is evaporate by simple technique such as by using vacuum pump, by the help of cold air stream, or by applying some heat.

Although small scale production of coprecipitates by this method is rather simple, large scale batches present many problems. These problems are solvent recovery, drying of the sample, uniformity in rates of evaporation, solvent flammability and toxicity, and batch reproducibility (15).

5.2 Lyophilization

A new method of preparing coprecipitates was reported by Gibbs et al. (31). The drug, an experimental tricyclic anti-depressant, and the carrier, poloxamer 407, were dissolved in dioxane, and the solvent was removed by lyophilization. The improvements in drug dissolution and absorption were evident.

Suvanakoot (30) demonstrated that solid dispersions of tolbutamide and phenylbutazone in PEG 20000 produced faster dissolution rates than the physical mixtures of the drugs with PEG 20000. By comparing three techniques of preparing the solid dispersions, it was found that freeze-drying technique gave the fastest dissolution rates for both drugs, followed by solvent method and melting method respectively. However, differences in dissolution rates among freeze-drying, direct melting, and solvent methods appeared to be very small. Freeze-drying offered the most rapid cooling process of all methods

available for preparing the solid dispersions. The particle size would be in an extremely fine state of subdivision due to the extremely high viscosity of the excipient at the low temperature and the short time interval for completion of solidification during freeze-drying.

McGinity (15) concluded that lyophilization appeared to be a very promising technique for large-scale productions, its use could eliminate several difficulties associated with the preparation of coprecipitates by the solvent method.

5.3 Spray Drying

Corrigan et al. (32) prepared solid dispersions of indomethacin, naproxen, ketoprofen, and ibuprofen in PVP by spray drying technique. Drug and PVP were dissolved in alcoholic solvent. The solvent was dried by spray drier. Samples prepared by co-spray drying indomethacin and PVP were amorphous. The release rate from the amorphous phase was over twenty times that observed from pure indomethacin. The physical stability of indomethacin as an amorphous phase improved when the drug was co-spray dried with PVP, the effect increased as the proportion of PVP in the solid increased. Co-spray drying naproxen, ketoprofen, or ibuprofen with sufficient PVP also gave amorphous solid products.

From the aforementioned study spray drying technique seems to be another choice for large-scale productions of coprecipitates. However, further investigations are needed in order to support this idea.

6. Fast-release Mechanism of Coprecipitates

Molecular or colloidal dispersion has been proposed as the mechanism for enhancement of dissolution and absorption rate of various drugs dispersed in some linear polymer (11,12,14). Molecular or colloidal dispersion can be achieved by coprecipitation in the form of interstitial solid solution (12). Goldberg et al. (9) suggested that a solid solution of a poorly soluble drug in a rapidly soluble carrier caused an improvement in dissolution rate because the particle size of the drug in the solid solution was reduced to a minimum state, i.e., its molecular size.

The limited solubility of a drug in another solid can arise in a number of ways. This may occur through substitution in the crystal lattice, occupation in an interstitial space or by fitting into sites of crystal imperfections. These are schematically illustrated in Figure 1.

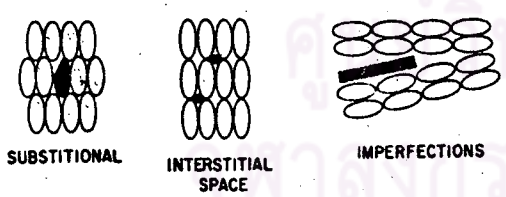


FIGURE 1. Schematic (2-dimensional) of the types of substitution which may occur in crystalline material.

Water-soluble crystalline polymers of high molecular weight appear to be logical choices for interstitial solid solutions. Polyethylene glycols, which are highly crystallite in nature, are believed to be capable of entrapping low molecular weight compounds in their interstitial space (12).

High viscosity of polymers is another factor which may contribute to the formation of metastable solid solutions (12). The crystallization of the drug is retarded due to reduced solute migration and the difficultly in nucleation of the drug in the viscous medium (11,12). The short interval of solidification is critical in formation of metastable solid solutions therefore, in the solvent method of preparation, the control of temperature and time of evaporation are very important to the final physical properties of the solid dispersions (11).

Molecular and colloidal dispersion also can be obtained by glass dispersion or glass solution (12). The lower density of glasses resulting from the molecular framework in the glasses could provide the environment for the dispersal of drug molecules. Such dispersions would be expected to rapidly dissolve in aqueous media. Drugs dispersed in glass matrices of dextrose, galactose, and sucrose have been reported to exhibit very rapid dissolution rates (13,33). Pure polyvinylpyrrolidone and some other polymers dissolved in the organic solvents may become glassy after the evaporation of the solvents (12).

The low lattice energy of the glass solution is another

reason for faster dissolution rate of the drug in the glass solution (12). Increasing in viscosity as the solvents evaporate may inhibit crystal growth resulting in the presence of the drug in a very fine state of subdivision (12).

The metastable nature of the glasses can be a problem, as they can undergo devitrification (crystallization). Citric acid has been shown to form glass dispersion systems with a number of drugs (11,34). These glasses will devitrify with time. However, the resulting dispersion is believed to contain the drug in a very fine state of subdivision.

During the process of forming a solid dispersion the individual components may precipitate in different solid phases from those present in a similar mixture i.e. as polymorphic, solvated, or amorphous phase. The physical forms produced are a function of the solidification technique, the solvent medium, the specific drug carrier system and the relative proportion of the components present (35).

If the new phases produced in the solid dispersion have a higher solubility, remain stable in the dispersion and do not rapidly revert to the less stable form on contact with dissolution medium, then enhanced dissolution from the dispersion over the mechanical mixture can be expected. The nature of the carrier plays an important role in maintaining the stability of many high energy drug phases.

Many carrier materials readily form soluble complexes with drugs thereby enhancing the drugs apparent solubility (12). Deshpande and Agrawal (36) prepared coprecipitates of chlorpropamide and PVP 10000, 44000 and 700000. They demonstrated that the increase in dissolution rate produced by the coprecipitates could be due to complex formation between the drug and PVP. PVP also has been found to form soluble complexes with hydroflumethiazide (37) and glibenclamide (38) during coprecipitation.

Water-soluble carriers themselves can improve the dissolution rate of poorly water-soluble drugs. The carrier material as it dissolves may have a solubilizing effect on the drug. This could be especially important in the diffusion layer surrounding the drug particles where saturated solutions of the drug would be found. The solubility of many compounds is known to be markedly increased in the presence of urea and other organic compounds (12,29).

In a coprecipitate where each crystallite of drug is surrounded by a water soluble crystals, there will be good wettability and dispersibility of the drug in the dissolution media. The enhanced wettability of the drug should retard any agglomeration or aggregation of the particles which can slow the dissolution process.

Quite often a coprecipitate does not entirely belong to any of the fast release mechanisms discussed but is made up of combinations of different mechanisms. The sulfathiazole dispersed at high concentration in PVP may be present as individual sulfathiazole and sulfathiazole-PVP complex molecules, amorphous and polymorphic

sulfathiazole, and possible an amorphous sulfathiazole-PVP complex (12).

7. Model for Dissolution of Molecular or Colloidal Dispersions

In solid dispersion system where the carrier dissolves bringing dispersed drug into the dissolution medium, drug release is dependent on the product of the carrier dissolution rate and the ratio of drug present (35).

$$G_d = \frac{G_c \cdot A_d}{A_c} \qquad \text{(Equation 1)}$$

G_d = The dissolution rate of the drug per unit surface area

G_c = The dissolution rate of the carrier per unit surface area

A = The component concentration in the system

Dissolution from high carrier weight fraction system of PVP-sulfathiazole (22) and PEG-drug (35) is consistent with equation 1.

Further confirmation of carrier controlled dissolution from PVP dispersions was obtained for hydrocortisone, prednisone, and clonazepam systems (35). It is apparent from equation 1 that if the presence of drug does not interfere with dissolution of the carrier, the absolute release rate of the different drugs at a given weight fraction should be the same. The relative change in drug dissolution rate becomes

$$\frac{G_d}{G_o} = \frac{G_c\ A_d}{G_o\ A_c} \qquad \text{(Equation 2)}$$

G_o = The intrinsic dissolution rate of the drug

Thus the relative rate of release from a given carrier is inversely proportion to the intrinsic dissolution rate (or solubility) of the drug.

7. Methods of Determination of Solid Dispersion Systems

Although characterization of the dispersion may not be required to satisfy regulatory agencies, it is necessary for evaluation of the drug's physical stability in the binary system and also for determination of the lot-to-lot reproducibility of a given physical type.

Differential thermal analysis, x-ray crystallography, infrared spectroscopy, microscopy, and dissolution rate studies can all be used to evaluate the dispersion in the powder and in the final dosage form.

9. Single Water-soluble Carriers

Over thirty different materials have been examined as potential carrier substances as shown in Table 1 (35). These carriers vary widely in chemical and physicochemical properties. A large proportion however are classified as either sugars, soluble polymers, surfactants or soluble acids.

Among those carriers, most of the reported investigations have focused on dispersions made with polyvinylpyrrolidone (PVP) and polyethylene glycols (PEG).

Table 1. Materials Tested as Carriers for Solid Dispersions

SUGARS	POLYMERIC MATERIALS	SURFACTANTS
Dextrose	Polyvinylpyrrolidone	Polyoxyethylene stearate
Sucrose	Polyvinylpolypyrrolidone	Renex 650
Galactose	Polyethylene glycols	Poloxamer 188
Sorbitol	Hydroxypropylmethylcellulose	Texafor ATP
Maltose	Methylcellulose	Deoxycholic acid
Xylitol	Pectin	Tweens
Mannitol	Hydroxyethylcellulose	Spans
Lactose	Hydroxypropylcellulose	
	Cyclodextrins	
	Galactomannan	

ACIDS	MISCELLANEOUS
Citric acid	Pentaerythritol
Succinic acid	Pentaerythrityltetraacetate
	Urea
	Hydroxyalkylxanthins
	Urethane

Polyethylene glycols can trap significant amounts of drug in their helical interstitial space. When PEG dispersions are prepared with their drug fraction greater than their solid solubility, ultrafine suspensions of the drug are produced. Although these dispersions exhibit much faster dissolution rates than the pure drug, they are relatively slower dissolving than those dispersions containing the drug in its molecularly dispersed form.

PEG polymer also acts as a protective colloid in retarding the coagulation, aggregation, or coarsening of the fine crystallites before solidification (12). The increasing viscosity imparted by PEG can inhibit drug crystal growth resulting in the presence of the drug in a very fine state of subdivision hence improving the drug dissolution.

10. Combined Water-soluble Carriers

In 1978, Allen et al. (20) prepared solid dispersion tablets of prednisone and hydrocortisone by using combined water-soluble carriers (50% sorbitol-50% mannitol, 50% sucrose-50% mannitol) and single water-soluble carrier (sorbitol, mannitol, sucrose). The result revealed that the solid dispersion tablets of the mannitol system had the fastest dissolution rate, followed by 50% sorbitol-50% mannitol, 50% sucrose-50% mannitol, sorbitol systems respectively.

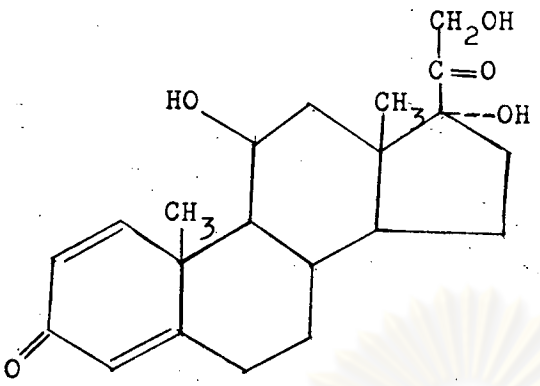
Later on Geneidi et al. (39) dispersed glibenclamide, by fusion method, in mannitol, sorbitol, 50% mannitol-50% sorbitol and found that solid dispersion systems of 50% mannitol-50% sorbitol produced the fastest dissolution rate of glibenclamide.

Mixture of sorbitol-mannitol (1:2) was also shown to be excellent water-soluble carriers for hydrochlorothiazide solid dispersion prepared by fusion method (40).

Miralles et al. (3) in 1982 conducted a study on the influences of single water-soluble carriers (dextrose, PEG 4000, PEG 6000, mannitol) and combined water-soluble carriers (dextrose-PEG 6000, mannitol-PEG 6000) on the dissolution rate of tolbutamide from its coprecipitates. Combined water-soluble carrier systems in various ratios were found to yield more improvement in dissolution rate of tolbutamide than single water-soluble systems.

From these investigations, combined water soluble systems seem to be a new trend of preparing solid dispersions in providing a better improvement in dissolution rate of an insoluble drug than single water-soluble carrier systems.

Prednisolone

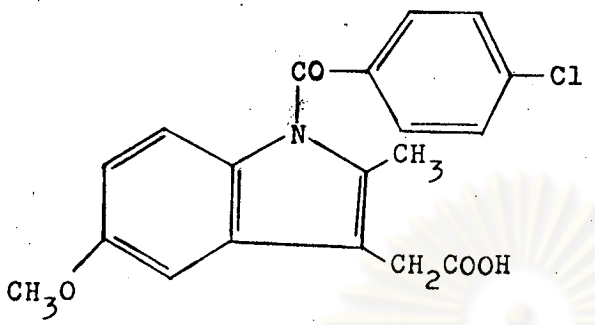


Prednisolone occurs as an odorless, white or almost white, crystalline hygroscopic powder with a bitter taste. Prednisolone exhibits melting point in the range of 230°C to 235°C. It decomposes to some degree at the melting point (7).

One gram of prednisolone dissolves in 1300 ml of water, 27 ml of dehydrated alcohol, 30 ml of alcohol.

Prednisolone is glucocorticoid. It has been included in a list of substances susceptible to biological problems (5). As a result, the USP requires a minimum dissolution rate for prednisolone tablets. The USP XX requires 60% dissolution in 20 minutes for prednisolone tablets (7).

Indomethacin



Indomethacin occurs as a pale yellow to yellow-tan crystalline powder. It shows polymorphism, one form melting at about 155° C and the other at about 162° C.

Indomethacin is practically insoluble in water. One gram of indomethacin dissolved in 50 ml of alcohol, 30 ml of chloroform, 40 ml of ether.

Indomethacin is a very low aqueous soluble drug. It has been widely used as anti-inflammatory analgesic in rheumatoid arthritis, spondylitis, and osteoarthritis, and to a lesser extent in gout. Its absorption is reported to be formulation dependence and the drug has been classified under demonstrating clinical inequivalence among its formulation (6). The USP XXI & NF XVI (2) requires 80% dissolution in 20 minutes for indomethacin capsules.

Anhydrous Dextrose

Anhydrous dextrose occurs as colorless crystals or as a white, crystalline or granular powder. It is odorless and has a sweet taste. Its melting point is about 83°C.

One gram of dextrose dissolves in about 1 ml of water and in about 100 ml of alcohol. It is more soluble in boiling water and in boiling alcohol.

Dextrose has long been utilized in the preparation of pharmaceutical dosage form, and the only difference in its past use and the newly proposed use is in the physical state. In the past, it has been used in physical mixtures, now it is suggested that it be used as a solid dispersion carrier in glassy state (33). The sugars enjoy many advantages over other forms of solid dispersion carriers because they are nontoxic, inexpensive, and physiologically acceptable.

Polyethylene Glycol 4000

Polyethylene glycol 4000 occurs as an almost tasteless, creamy-white, hard, wax-like solid or flakes or white free flowing powder with a faint characteristec odor. Its melting point is in the range of 53°C to 56°C and it remains stable up to 135°C. It exhibits viscosity of 76 to 110 centistokes at 100°C.

One gram of PEG 4000 dissolves in 3 ml of water, 2 ml of alcohol, 2 ml of chloroform. It is practically insoluble in ether, but soluble in many organic solvents.

Polyethylene glycol 4000 is a lubricant in tablet formulation. It has been used as a water-soluble carrier in preparing coprecipitates of some drugs such as diazepam (16), tolbutamide (3).

Sodium Lauryl Sulfate (SLS)

Sodium lauryl sulfate occurs as white or light-yellow crystals or flakes having a slight coconut fatty odor.

One gram of sodium lauryl sulfate dissolves in 10 ml water, forming an opalescent solution. It is practically insoluble in chloroform, ether, and light petrolatum.

Sodium lauryl sulfate is a surfactant and is also used as a lubricant in tablet formulation. It has been incorporated into tablets of some poorly soluble drugs to improve their dissolutions.