The International Journal of Health Research is an online international journal allowing free unlimited access to abstract and full-text of published articles. The journal is devoted to the promotion of health sciences and related disciplines (including medicine, pharmacy, nursing, biotechnology, cell and molecular biology, and related engineering fields). It seeks particularly (but not exclusively) to encourage multidisciplinary research and collaboration among scientists, the industry and the healthcare professionals. It will also provide an international forum for the communication and evaluation of data, methods and findings in health sciences and related disciplines. The journal welcomes original research papers, reviews and case reports on current topics of special interest and relevance. All manuscripts will be subject to rapid peer review. Those of high quality (not previously published and not under consideration for publication) will be published without delay. The maximum length of manuscripts should normally be 10,000 words (20 single-spaced typewritten pages) for review, 6,000 words for research articles, 3,000 for technical notes, case reports, commentaries and short communications.

**Submission of Manuscript:** The International Journal of Health Research uses a journal management software to allow authors track the changes to their submission. All manuscripts must be in MS Word and in English and should be submitted online at http://www.ijhr.org. Authors who do not want to submit online or cannot submit online should send their manuscript by e-mail attachment (in single file) to the editorial office below. Submission of a manuscript is an indication that the content has not been published or under consideration for publication elsewhere. Authors may submit the names of expert reviewers or those they do not want to review their papers.

**Enquiries:**

The Editorial Office  
International Journal of Health Research  
Dean’s Office, College of Medicine  
Madonna University, Elele Campus, Rivers State  
E-mail: editor_ijhr@yahoo.com or editor@ijhr.org
Review Article

Dissolution Enhancement of Drugs.
Part I: Technologies and Effect of Carriers

Received: 03-Dec-08 Revised: 12-Apr-09 Accepted: 05-May-09

Abstract

For complete absorption and good bioavailability of orally administered drug, the drug must be dissolved in gastric fluids. Dissolution of drug is the rate-controlling step which determines the rate and degree of absorption. Drugs with slow dissolution rates generally show erratic and incomplete absorption leading to low bioavailability when administered orally. Since aqueous solubility and slow dissolution rate of BCS class II and class IV drugs is a major challenge in the drug development and delivery processes, improving aqueous solubility and slow dissolution of BCS Class II and Class IV drugs have been investigated extensively. Various techniques have been used in attempt to improve solubility and dissolution rates of poorly water soluble drugs which include solid dispersion, micronization, lipid based formulations, melt granulation, direct compaction, solvent evaporation, coprecipitation, adsorption, ordered mixing, liquisolid compacts, solvent deposition inclusion complexation and steam aided granulation. In these techniques carrier plays an important role in improving solubility and dissolution rate. Polymers, superdisintegrants, surfactants are extensively studied in recent years for dissolution enhancement in drugs. This part of this review discusses technological overview and effect of polymers, superdisintegrants and surfactants on dissolution enhancement of drugs while Part II [Int J Health Res, Sept 2009; 2(3)] describes the role and applications of cyclodextrins, carbohydrates, hydrotropes, polyglycolized glycerides, dendrimers, acids and miscellaneous carriers in enhancing dissolution of drugs.

Keywords: Dissolution enhancement; aqueous solubility, water soluble carriers; BCS class II, excipients.

Vikas A Saharan
Vipin Kukkar
Mahesh Kataria
Manoj Gera
Pratim K Choudhury

1Institute of Pharmaceutical Sciences and Drug Research, Seth GL Bihani SD College of Technical Education, Sri Ganganagar, Rajasthan, India

2Department of Pharmaceutical Sciences, ML Sukhadia University, Udaipur, Rajasthan, India

For Correspondence:
Vikas A Saharan, Assistant Professor and In charge, Committee for Higher Education Guidance (GATE Cell), Seth G. L. Bihani S. D. College of Technical Education, Gaganpath, Sri Ganganagar, Rajasthan, India.

Mobile: +91-9799299706
Tel: +91-154-2466777
Fax: +91-154-2466774

Email: vikas.pharmaceutics@gmail.com
Introduction

Nearly one-third of drugs in development are water insoluble and one-half fail in trials because of underprivileged pharmacokinetics [1]. These poorly water soluble drugs are allied with slow drug absorption leading to inadequate and variable bioavailability and G.I. mucosal toxicity of drugs [2]. Poorly water soluble drugs belong to BCS class II and Class IV [3] group of compounds. In the process of absorption of drug from oral route dissolution is the rate limiting step for lipophilic drugs. Therefore it is necessary to enhance dissolution of these drugs to ensure maximum therapeutic utility of these drugs. Before studying the various approaches to enhance dissolution it is necessary to understand the basic process of dissolution. Dissolution is a process by which a solid substance goes into solution. The extent to which the dissolution proceeds, under a given set of conditions is referred to as the solubility of the substance in the solvent i.e. rate of solution (dissolution) and amount that can be dissolved (solubility) are not same. The dissolution rate of a drug is directly proportional to its solubility as per Noyes-Whitney equation and therefore solubility of a drug substance is a major factor that determines its dissolution rate and hence its absorption and bioavailability eventually [4].

The various properties of drug that affect drug dissolution and its rate includes solubility, particle size, polymorphism, salt form, complexation, wettability, etc [5] and can be targeted to enhance dissolution of poorly water soluble drugs. Use of water soluble excipients is common and simplest way to enhance dissolution rate of hydrophobic drugs. These excipients namely polymers, superdisintegrants, carbohydrates, surfactants hydrotropes, acids etc work in different ways to enhance water solubility of drugs. The role of techniques of preparation of formulation is as imperative as the choice of the carriers to enhance dissolution of drugs due to difference in reduction of crystallinity of the product and surface characteristics of the particles. Part I of this review highlights various dissolution enhancement techniques for poorly water soluble drugs as well as role of few water soluble carriers, viz. polymers, superdisintegrants and surfactants, in dissolution enhancement. While part II [Int J Health Res, Sept 2009; 2(3)] describes use of cyclodextrins, carbohydrates, hydrotropes, polyglycolized glycerides, dendrimers, acids and miscellaneous carriers in enhancing dissolution of drugs.

Techniques for Dissolution Enhancement

There are several techniques reported in literature for formulation of hydrophobic drugs with enhanced dissolution rate. These techniques are carefully selected on the basis of properties of drug, excipients and dosage forms.

Solid Dispersion

Solid dispersion is defined as a dispersion of one or more active ingredients in an inert carrier or matrix at solid state prepared by the melting (fusion), solvent, or melting-solvent method [6]. In melting method carrier is melted and drug is added with stirring and melted until homogenous melt is obtained which is then cooled to room temperature while in solvent method drug and carrier is dissolved in minimum amount of solvent and solvent is removed by evaporation under reduced pressure [7]. Solid dispersions are also prepared by dissolving drug and carrier in a common solvent followed by evaporation of the solvent. Melting-solvent method involves use of heating and solvent action to dissolve the drug and carrier in solvent followed by evaporation of the solvent. Solid dispersion technique improves the solubility, dissolution rate, and as a result the bioavailability of poorly water-soluble drugs [8].
The higher dissolution rates of solid dispersions can be ascribed to a number of factors which includes:

1. The formation of higher energy metastable states of the components as a function of the carrier system being used and the proportion of carriers present [9].
2. The reduction of particle size to nearly a molecular level [10]. As the soluble carrier dissolves, the insoluble drug is exposed to dissolution medium as very fine particles leading to an increase in both surface area and solubilization for fast dissolution and absorption [6].
4. The presence of carrier may also prevent aggregation of fine drug particles, thereby providing a larger surface area for dissolution. The wetting properties are also greatly increased due to the surfactant property of the polymer, resulting in decreased interfacial tension between the medium and the drug, hence higher dissolution rates. The presence of carrier polymers also inhibits crystal growth of the drug which facilitates faster dissolution [9].
6. Intermolecular hydrogen bonds between drug and carrier [12].
7. Local solubilization effect of carrier at the diffusion layer [7].

Various factors affecting dissolution of drug from solid dispersion includes the method of preparation of the solid dispersion, amount and properties of the polymer carriers, drug polymer contact and drug-polymer interactions [13].

**Inclusion Complexation**

This is most widely used method to enhance water solubility and increase stability of hydrophobic drugs by using cyclodextrins.

Solid inclusion complexes can be prepared by using following methods:

a) **Kneading Technique**

In this technique, cyclodextrin (CD) is impregnated with water and converted to paste. Drug is then added and kneaded for specified time. The kneaded mixture is then dried and passed through sieve if required [14].

b) **Coprecipitation**

Required amount of drug is added to the solution of β-CD. The system is kept under magnetic agitation with controlled process parameters and protected from the light. The formed precipitate is separated by vacuum filtration and dried at room temperature in order to avoid the loss of the structure water from the inclusion complex [15].

c) **Neutralization**

Drug is added in alkaline solution like sodium hydroxide, ammonium hydroxide. A solution of β- Cyclodextrin is then added to dissolve the joined drug. The clear solution obtained after few seconds under agitation is neutralized using HCl solution until reaching the equivalence point. At this moment, the appearance of a white precipitate could be appreciated, corresponding to the formation of the inclusion compound. The precipitate is then filtered and dried [16].

d) **Co-grinding**

Drug and cyclodextrin are mixed and the physical mixture is introduced in a suitable mill like oscillatory mill and grinded for suitable time [15].

e) **Spray-Drying Method**

Drug is dissolved in suitable solvent and the required stoichiometric amount of carrier material like β cyclodextrin is dissolved in water. Solutions are then mixed by sonication or other suitable method to
produce a clear solution, which is then spray-dried using spray dryer [15].

**f) Microwave Irradiation Method**

Drug and cyclodextrins mixture is reacted in microwave oven to form inclusion. It is a novel method for industrial scale preparation due to its major advantage of shorter reaction time and higher yield of product [17].

**Steam-Aided Granulation**

Steam instead of water can be used in wet granulation because it provides a higher diffusion rate into the powder and a more favorable thermal balance during the drying step. After condensation of the steam, water forms a hot thin film, requiring only a small amount of extra energy for its elimination and evaporates more easily. The use of steam instead of liquid water in a wet granulation method can considerably decrease the amount of water used and as a result the whole operational time [18].

**Cogrinding / Comicronization**

Cogrinding of a poorly water-soluble drug with water-soluble polymers like hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA) etc in the presence of small amount of water is extremely effective to improve its apparent solubility with maintenance of drug crystallinity to some extent [19]. Small particles produced by milling or micronization have increased surface area and expected to have enhanced dissolution rate. However, energy added to reduce particle size results in increased van der Waal's interactions and electrostatic attraction between particles leading to reduce effective surface area due to agglomeration thus decreasing dissolution rate. Micronization of drugs by using excipients like microcrystalline cellulose can be used as an alternative to reduce or eliminate cohesive and electrostatic forces. This approach increases apparent surface area available for drug dissolution by creating an ordered mixture, thereby causing a reduction in particle-particle agglomeration or by reducing van der Waal's interactions. Increase in true surface area of the ordered powdered mixture is expected due to the inherent surface roughness and porosity of the microcrystalline cellulose-drug mixture [20].

**Lipid-based formulations**

Lipid-based delivery systems like emulsions, microemulsions, liposomes, microspheres, solid-lipid nanoparticles, etc have ability to avoid resistant chemical and physical barriers to oral absorption and are most successful in enhancing the bioavailability of molecules that are poorly water-soluble but highly permeable drug molecules (BCS class II). Some proposed mechanisms of action of lipid-based systems to enhance oral bioavailability of compounds include [21]:

a) Particle size reduction to molecular size yielding a solid-state solution within the carrier.

b) Enhanced wetting of hydrophobic solids resulting in enhanced dissolution.

c) Increased rate of dissolution into aqueous environment from oil droplets of high surface area.

d) Promotion of absorption via intrinsic lipid pathways.

e) Enhanced thermodynamic activity via supersaturation of the aqueous environment of the gastrointestinal tract.

**Melt-Granulation**

In this technique powdered drugs are efficiently agglomerated by the use of a meltable binder which can be a molten liquid, a solid or a solid that melts during the process usually in high shear mixers, where the product temperature is raised higher than the melting point of the binder either by a heating jacket or, when the impeller speed is high enough, by the heat of friction generated by the impeller blades [22]. In this technique no water or organic solvents are
needed and there is no drying step therefore the process is environmentally safe, less time consuming and uses less energy than conventional wet granulation [23]. Polyethylene glycol is widely used as a molten binder due to its complimentary solution properties, low melting point, rapid solidification rate, low toxicity and little cost [22]. The increase in dissolution rate can be ascribed to the hydrophilic character of the system due to the presence of water-soluble carriers and the fact that the drug forms monotectic mixtures with PEG [23].

**Direct Compaction**

In this process polymer like hydroxypropyl methylcellulose and drug is dry-blended, compressed into slugs and then milled into a granular powder. The process results in enhanced dissolution rate of poorly water-soluble drugs without the use of solvent or heat addition to overcome the disadvantages of solid dispersion by these methods. This process is also cost effective and quicker. The compaction processes are believed to be particularly effective at enhancing the rate of drug dissolution because the drug particles are maintained in direct contact with the polymer particles during drug dissolution, in contrast with a physical mixture where the drug and polymer particles may rapidly disperse and be separated in the dissolution medium [24].

**Solvent Evaporation by Ultra-Rapid Freezing (URF)**

This process involves freezing a drug contained in a polymer solution onto the surface of a cryogen substrate with a thermal conductivity (k) between 10 and 20 W/(m K), collecting the frozen particles and removing the solvent. Because of rapid conductive heat transfer, resulting in high supersaturation and nucleation rates, the URF technology has the potential to create powders with superior physicochemical properties, similar to those produced by other rapid freezing technologies. As in other freezing technologies, the rapid freezing of the drug/polymer composition is decisive in preventing phase separation during freezing, allowing for the active to be molecularly dispersed with the polymer. Recrystallization of the drug is avoided by the inclusion of high glass-transition temperature (Tg) polymers such as PVP or hypromellose (HPMC). This technique is widely applicable to enhance in-vivo absorption for the BCS class II compounds [25].

**Coevaporate System / Coprecipitation**

Weak basic drugs like prochlorperazine maleate contain good solubility in acidic pH but in alkaline pH solubility is significantly reduced and when a conventional formulation containing weak base is given orally precipitation of poorly soluble free base occurs within formulation in intestinal fluid. Precipitated drug is no longer capable of release from formulation leading to decrease in bioavailability of drug. This problem can be solved by use of coevaporate system which incorporates a carrier with solubilizing effect in alkaline intestinal fluid which may operate in the microenvironment, immediately surrounding the drug particle and polymers for controlling the dissolution rate to formulate dosage forms ensuring maximum bioavailability with controlled release of weak base [26].

**Ordered/Interactive Mixing**

Ordered mixing is described as method to prepare ordered units in the mix such that the ordered unit will be the smallest possible sample of the mix and will be of near identical composition to all the other ordered units in the mix. Ordered mixing yields nearly the perfect mix and may be obtained in a number of ways like mechanical means, adhesion, coating and other methods [27]. Prerequisite for fast dissolution from an ordered mixture includes that the carrier particle should dissolve rapidly, delivering a fine particulate suspension of drug particles [28]. Higher concentration of drug shows reduced dissolution rates particularly at loadings above monolayer coverage.
because high concentration of drug forms agglomerates rather than discrete particles with resulting decreased surface area and thicker diffusional layers causing reduction in dissolution rates [29]. In an ordered powder mix fine drug particles are distributed fairly evenly on coarse carrier particles. The drug powder is therefore deagglomerated in the dry state. This may be used to increase the dissolution rate of drug powders because a larger contact surface area is exposed to the dissolution medium [28].

Adsorption of Drugs onto High Surface Area Carriers

In this technique drug is absorbed onto carriers having large surface area (like crosslinked polyvinylpyrrolidone, Kollidone) from solutions of the drug in appropriate solvents like methanol, polyethylene glycol, and 2-pyrolidone. The dissolution rate of drug increases due to increase in surface area and drug particles have good wettability due to the surrounding solubilising materials [30].

Liquisolid Compacts

Liquid Compacts are compressible powdered forms of liquid medications. The term “liquisolid medication” implies oily liquid drugs and solutions or suspensions of water-insoluble drugs carried in suitable non-volatile solvent systems. Using this technique, a liquid medication may be converted into a dry, non-adherent, free flowing and compressible powder by a simple blending with selected powder excipients such as the carrier and coating material. Surfactants like tweens are used to improve aqueous solubility of poorly soluble drugs [31].

Solvent Deposition / Evaporation

In this technique drug is dissolved in a solvent like methylene chloride to produce a clear solution. The carrier is then dispersed in the solution by stirring and the solvent is removed by evaporation under temperature and pressure. The resultant mass is then dried, pulverized, and passed through a sieve. The Increase in the dissolution rate is ascribed to the reduced particle size of the drug deposited on the carrier and enhanced wettability of the particles brought about by the carrier [32].

Carriers for Dissolution Enhancement

Carriers, which are soluble and dissolve in water at a fast rate, are widely used in pharmaceutical formulations to enhance dissolution of drugs. The carriers which have been reported in literature are presented in Table 1 and are described in detail under different categories.

Polymers

Polymers like polyethylene glycols (PEGs), hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), polyvinylpyrrolidone (PVP) etc when used in optimum concentration lead to increase in dissolution rate due to reduction in particle size, solubilization effect of the carrier, increase wettability and dispersibility, formation of hydrogen bonds between drug and carrier (Table 2). When polymers are used in higher proportion these can decrease dissolution rate due to leaching out of the carrier during dissolution which might form a concentrated layer of solution around the drug particles and the migration of the released drug particles to the bulk of the dissolution medium slows down [12].

Solid dispersions (SDs) of glyburide were prepared using PEG 4000, PEG 6000 and a mixture of PEG 4000 and PEG 6000 (1:1 ratio) by fusion and solvent method and selected solid dispersions were lyophilized. The dispersion containing glyburide/PEG 6000, 1:8, showed 14-fold increase in dissolution and dispersion containing glyburide/PEG 4000, 1:10, showed an 8-fold and dispersion containing 6 parts of PEG mixture show 12-fold increase as compared with pure drug. Lyophilization of solid dispersions further supplement dissolution
Table 1: Classification of carriers enhancing dissolution of drugs

<table>
<thead>
<tr>
<th>S/N</th>
<th>Category</th>
<th>Example of carriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Polymers</td>
<td>Polyvinylpyrrolidone, Polyelectrolyte, Polyethylene glycol, Hydroxyethyl cellulose, Poly (2-hydroxyethylmethacrylate), Methacrylic copolymers (Eudragit® S100 sodium salts and Eudragit® L100 sodium salts)</td>
</tr>
<tr>
<td>2.</td>
<td>Superdisintegrants</td>
<td>Sodium starch glycolate, Croscarmellose sodium, Cross-linked polyvinylpyrrolidone, Cross-linked alginic acid, Gellan gum, Xanthan gum, Calcium silicate</td>
</tr>
<tr>
<td>3.</td>
<td>Cyclodextrins</td>
<td>β-Cyclodextrins, Hydroxypropyl-β-cyclodextrins</td>
</tr>
<tr>
<td>4.</td>
<td>Carbohydrates</td>
<td>Lactose, Soluble starch, Sorbitol, Mannitol, β-(1-4)-2-amino-2-deoxy-D-glucose (Chitosan), Maltose, Galactose, Xylitol, Galactomannan, British gum, Amylodextrin</td>
</tr>
<tr>
<td>5.</td>
<td>Surfactants</td>
<td>Poloxamers (Lutrol® F 127, Lutrol® F 68), Polyglycolized glyceride (Labrasol), Polyoxyethylene sorbitan monoesters (Twens), Sorbitan esters (Spans), Polyoxyethylene stearates, Poly (beta-benzyl-L-aspartate) -b- poly (ethylene oxide), Poly (caprolactone) -b- poly (ethylene oxide)</td>
</tr>
<tr>
<td>6.</td>
<td>Hydrotropes</td>
<td>Urea, Nicotinamide, Sodium benzoate, Sodium salicylate, Sodium acetate, Sodium-o-hydroxy benzoate, Sodium-p-hydroxy benzoate, Sodium citrate</td>
</tr>
<tr>
<td>7.</td>
<td>Polyglycolized glycerides</td>
<td>Gelucire 44/14, Gelucire 50/13, Gelucire 62/05</td>
</tr>
<tr>
<td>8.</td>
<td>Acids</td>
<td>Citric acid, Succinic acid, Phosphoric acid</td>
</tr>
<tr>
<td>9.</td>
<td>Dendrimers</td>
<td>Starburst® polyamidoamine (PAMAM)</td>
</tr>
<tr>
<td>10.</td>
<td>Miscellaneous</td>
<td>Microcrystalline cellulose, Dicalcium phosphate, Silica gel, Sodium chloride, Skimmed milk</td>
</tr>
</tbody>
</table>

due to increase in surface area and hence surface free energy [9].

Solid dispersions of norfloxacin with PEG 6000 in weight ratios of 10:90, 20:80, 30:70 and 50:50 were prepared by fusion method. Solubility studies revealed no significant increase in solubility of norfloxacin on addition of PEG. Dissolution studies showed maximum dissolution rate of drug with PEG 6000 in 30:70 and 20:80 weight ratios establishing the effect and importance of optimum weight fraction of polymer [33].

Solid dispersions of piroxicam were prepared using polyvinylpyrrolidone K-30 in 1:0.5, 1:1, 1:2, 1:3, 1:5 and 1:6 ratio of drug to polymer by solvent method. The dissolution of drug in solid dispersion was dependent on drug to PVP ratio. The drug:PVP in 1:4 ratio, solid dispersion gave highest dissolution rate of about a 38-fold higher than that of pure drug [12].

Carbamazepine/PEG 4000 and PEG 6000 solid dispersions were prepared by the fusion method involving heating a physical mixture of carbamazepine and either PEG 4000 or PEG 6000 in 1:2, 1:4, 1:6 and 1:8 drug/carrier ratios, to the liquid state. Dissolution studies suggested that the dissolution of carbamazepine from the solid dispersion was neither related to the molecular weight nor the weight fraction of PEG. The enhancement in dissolution of solid dispersion may be ascribed to complex formation between carbamazepine and PEG 6000 during melting and a polymorphic change during the preparation of solid dispersion with carbamazepine crystallizing in
### Dissolution Enhancement of Drugs

**Table 2:** Polymers and techniques employed for enhancing dissolution of poorly water soluble drugs

<table>
<thead>
<tr>
<th>S/N</th>
<th>Drug</th>
<th>Polymer</th>
<th>Technique</th>
<th>Mechanism of Dissolution Enhancement</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Glyburide</td>
<td>PEG 4000, PEG 6000 and there mixtures</td>
<td>Solid dispersion by fusion and solvent method</td>
<td>Increase in surface area and hence surface free energy resulting in an increase in the dissolution</td>
<td>(9)</td>
</tr>
<tr>
<td>2.</td>
<td>Norfloxacin</td>
<td>PEG 6000</td>
<td>Solid dispersion by fusion method</td>
<td>Solubilizing effect of PEG on the drug</td>
<td>(33)</td>
</tr>
<tr>
<td>3.</td>
<td>Piroxicam</td>
<td>PVP K-30</td>
<td>Solid dispersion by solvent method</td>
<td>Increase in drug wettability and the presence of intermolecular hydrogen bonds between piroxicam and PVP</td>
<td>(12)</td>
</tr>
<tr>
<td>4.</td>
<td>Carbamazepine</td>
<td>PEG 4000 and PEG 6000</td>
<td>Solid dispersion by fusion method</td>
<td>Complex formation between carbamazepine and PEGs during melting and a polymorphic change during the preparation of solid dispersion, with carbamazepine crystallizing in a metastable form of higher dissolution rate</td>
<td>(34)</td>
</tr>
<tr>
<td>5.</td>
<td>Piroxicam</td>
<td>PEG 4000</td>
<td>Solid dispersion by fusion and solvent method</td>
<td>Increased wettability of drug, a local solubilization effect of carrier at the diffusion layer, formation of amorphous phase of piroxicam and particle size reduction resulted from interaction of drug and PEG 4000</td>
<td>(7)</td>
</tr>
<tr>
<td>6.</td>
<td>Flurbiprofen</td>
<td>Polyvinyl pyrrolidone (PVP), Hydroxypropyl methylcellulose (HPMC), Hydroxypropyl cellulose (HPC), Poly ethylene glycol (PEG) 6000</td>
<td>Solid dispersion by solvent method</td>
<td>Particle size reduction, improved wettability of drug particle by the carriers, solubilizing effect of carrier and possible conversion of crystalline drug into amorphous form</td>
<td>(35)</td>
</tr>
<tr>
<td>7.</td>
<td>Glibenclamide</td>
<td>PEG 6000</td>
<td>Solid dispersion by fusion method</td>
<td>Solubilizing effect of PEG on the drug</td>
<td>(36)</td>
</tr>
<tr>
<td>8.</td>
<td>Roxithromycin</td>
<td>PEG 6000, HPMC K4M and HPC</td>
<td>Solid dispersion by coprecipitate method</td>
<td>Reduction of particle size of the drug and surface tension lowering effect of carriers resulting in wetting of hydrophobic roxithromycin surface</td>
<td>(10)</td>
</tr>
<tr>
<td>9.</td>
<td>Gliclazide</td>
<td>PEG 4000 and PEG 6000</td>
<td>Solid dispersion by solvent method</td>
<td>Reduction of particle size resulting in enhancement of surface area and increase in drug wettability</td>
<td>(8)</td>
</tr>
<tr>
<td>S/N</td>
<td>Drug</td>
<td>Polymer</td>
<td>Technique</td>
<td>Mechanism of Dissolution Enhancement</td>
<td>Reference</td>
</tr>
<tr>
<td>-----</td>
<td>----------------------------------------</td>
<td>--------------------------------------</td>
<td>---------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>10.</td>
<td>Albendazole</td>
<td>PEG 6000</td>
<td>Solid dispersion by fusion, solvent and kneading method</td>
<td>Increased surface area for mass transfer, thermodynamically enhanced dissolution of a higher energy amorphous form from the carrier, improved wetting and solubilization</td>
<td>(37)</td>
</tr>
<tr>
<td>11.</td>
<td>Rofecoxib</td>
<td>PEG 4000, PEG 6000, PVP K25</td>
<td>Solid dispersion by hot-melt method</td>
<td>Formation of interstitial solid solutions</td>
<td>(2)</td>
</tr>
<tr>
<td>12.</td>
<td>Diclofenac sodium, Naproxen and Piroxicam</td>
<td>Poly (2-hydroxyethylmethacrylate) (PHEMA)</td>
<td>Solid dispersion by solvent method</td>
<td>Conversion of crystalline drug into amorphous form having higher aqueous solubility</td>
<td>(38)</td>
</tr>
<tr>
<td>13.</td>
<td>Nifedipine, Griseofulvin, Indomethacin</td>
<td>PEG 6000-HPMC</td>
<td>Cogrinding</td>
<td>Interaction between drug and polymer resulting in highly polar environment</td>
<td>(19)</td>
</tr>
<tr>
<td>14.</td>
<td>Piroxicam</td>
<td>PEG 4600</td>
<td>Lipid based formulations</td>
<td>Solubilizing effect of PEG on the drug</td>
<td>(21)</td>
</tr>
<tr>
<td>15.</td>
<td>Carbamazepine</td>
<td>PEG 4000</td>
<td>Melt granulation</td>
<td>Solubilizing effect of PEG on the drug</td>
<td>(22)</td>
</tr>
<tr>
<td>16.</td>
<td>Griseofulvin</td>
<td>PEG 3350, Gelucire 44/14</td>
<td>Melt granulation</td>
<td>Higher hydrophilic character of the system due to the presence of water-soluble carriers and part of the drug dissolved in the binder</td>
<td>(23)</td>
</tr>
<tr>
<td>17.</td>
<td>Naproxen, Nifedipine, Carbamazepine</td>
<td>HPMC USP Type 2208 (K3LV), HPMC USP Type 2910 (E3LV and E5LV)</td>
<td>Compaction process</td>
<td>Microenvironment surfactant effect where by HPMC dissolution creates a local surfactant concentration in the boundary layer surrounding the drug particles, providing a lower energy pathway for drug dissolution</td>
<td>(24)</td>
</tr>
<tr>
<td>18.</td>
<td>Micronized danazol</td>
<td>PVP K-15</td>
<td>Ultra-rapid freezing</td>
<td>Increase in solubility driving force, lowering the heat of solution of the danazol, nano-structured amorphous drug domain, and improved surface area.</td>
<td>(25)</td>
</tr>
<tr>
<td>19.</td>
<td>Prochlorperazine maleate</td>
<td>HPMC</td>
<td>Coevaporates</td>
<td>Solubilization effect of carrier</td>
<td>(26)</td>
</tr>
<tr>
<td>20.</td>
<td>Piroxicam</td>
<td>Eudragit® L100 sodium salts (EuLNa) and Eudragit® S100 sodium salts (EuSNa)</td>
<td>Fast-dissolving mucoadhesive microparticulate delivery system</td>
<td>Mucoadhesive properties of carriers and increase apparent drug solubility</td>
<td>(39)</td>
</tr>
</tbody>
</table>
a metastable form of higher dissolution rate [34].

Solid dispersions of piroxicam in PEG 4000 at 1:1, 1:2 and 1:3 ratio of drug to polymer were prepared by fusion and solvent method with enhanced dissolution due to increased wettability of drug, a local solubilization effect of carrier at the diffusion layer, formation of amorphous phase of piroxicam and particle size reduction resulted from interaction of drug and PEG 4000. Storage stability studies at 25°C and 37°C for 10 weeks showed that all dispersions were stable except that uptake of water during storage may occur in PEG system which leads to decrease of piroxicam potency in piroxicam-PEG solid dispersions [7].

Solid dispersions of flurbiprofen in PVP, HPMC, HPC and PEG 6000 in 19:1 and 9:1 ratio of drug to carrier were prepared by solvent method. Among these polymers PVP gave highest enhancement (19-fold) in the dissolution rate of flurbiprofen at 9:1 drug to carrier ratio. The dissolution rate of flurbiprofen with various polymer solutions was in the descending order of PVP, HPMC, PEG, and HPC at 9:1 ratio of drug to carrier. As concentration of carrier in solid dispersion was increased, the rate of dissolution was also increased with PVP and HPMC while decreased with HPC and PEG 6000 due to aggregation of drug and carrier in solid dispersion [35].

Solid dispersions of glibenclamide were prepared using PEG 6000 by fusion method. Dissolution studies revealed enhanced dissolution of glibenclamide compared with marketed daonil[R] tablets (Hoechst) due to improved wettability and dispersibility of drug from solid dispersion [36]. Solid dispersions of roxithromycin were prepared using PEG, HPMC and HPC in 1:1, 1:3, and 1:5 ratio of drug to polymer by coprecipitate method. The dissolution rate of roxithromycin solid dispersions was in the descending order of PEG, HPMC, HPC and PEG showed highest dissolution at 1:5 drug to PEG ratio. Solubility of roxithromycin was directly proportional to the increment in concentration of polymers from 0.5 to 3 % polymer solution. Angle of repose and carr's index studies indicated fine nature and good flow properties of the all formulations [10].

Solid dispersions of gliclazide were prepared using PEG 4000 and PEG 6000 in 1:1, 1:3, and 1:5 ratio of drug to polymer by solvent method using chloroform as solvent. Drug: carrier ratio of 1:5 was found to be optimum for improving dissolution rate of gliclazide for both polymer systems and PEG 6000 solid dispersions showed faster dissolution than PEG 4000 solid dispersions [8]. Solid dispersions of albendazole were prepared using PEG 6000 in 1:1, 1:3 and 1:5 ratio of drug to polymer by fusion, solvent and kneading method. Solid dispersions improved dissolution compared to physical mixtures owing to increased surface area for mass transfer, thermodynamically enhanced dissolution of a higher energy amorphous form from the carrier, improved wetting and solubilization of the drug [37].

Solid dispersions of rofecoxib with PVP, PEG 4000 and PEG 6000 in 50%, 75% and 90% w/w were prepared by hot-melt method. The solubility efficiency of polymers was in the order of PVP >> PEG 4000 > PEG 6000 due to high amorphizing properties of PVP than the PEGs. Significant dissolution improvement was observed at the highest carrier amount i.e. 90% and was ascribed to the formation of interstitial solid solutions [2].

Solid molecular dispersion of diclofenac sodium, naproxen and piroxicam using Poly (2-hydroxyethylmethacrylate) (PHEMA) hydrogel as carrier were prepared by solvent method using 90:10 ethanol:water for diclofenac sodium, 100% ethanol for naproxen, and 100% acetone for piroxicam. The results showed threshold drug loading level of about 30% in these solid dispersions, above which amorphous to crystalline transition may occur. The presence of hydrogen bonding between drug and polymer improves the compatibility between
drug and polymer. Stability studies under varying conditions of humidity (22-92 RH %) showed transition from clear sample to an opaque one on increasing humidity due to increased mobility in the glassy PHEMA matrix and solid dispersion remains in amorphous form longer at low relative humidity [38].

Coground mixtures of nifedipine, griseofulvin, and indomethacin were prepared by dispersing drug in the fused PEG 6000 and then adding HPMC, MC, and PVA polymers to the mixture. After cooling to room temperature, the solidified mass was ground using a ball mill. Then solvent like water, methanol, ethanol, dichloromethane was added to observe the effect of solvents and further ground and dried to remove solvent. The resultant mass was lightly pulverized to pass through a 200 µm screen. Hydroxyl groups in the water-soluble polymer participate in the solubility enhancement and some interactions between drug and the polymer occurs during the cogrinding process through the functional groups in a small amount of water added (highly polar environment). Solubility also increased in the presence of organic solvents suggesting that the pulverizing effect for drugs like nifedipine also promote the drug-polymer interactions [19].

Lipid based formulations of piroxicam were prepared using 1,2-dimyristoyl-sn-glycero-3-phosphatidylcholine (DMPC) phospholipids alone in 1:1 and 2:1 ratio of drug:DMPC and a mixture of DMPC and PEG 4600 in 2:1 ratio. Dissolution studies showed highest increase in drug release from combination of lipid with PEG as compared to lipid alone due to solubilizing effect of PEG on the drug thus enhancing the dissolution rate. Storage stability studies at 4°, 25° and 60°C revealed stability of at least 6 months but beyond this decrease in dissolution rates for formulations containing PEG 4600 due to formation of a crystalline mass upon storage for extended period. Stabilizers like polyvinyl alcohols can be added to increase storage stability of all these preparations [21].

Fast release rate formulation of carbamazepine was prepared by melt granulation technique using PEG 4000 as a melt binder without using solvents or water. Solid-state analysis indicated only a limited reduction of the crystallinity of the drug and no changes in its polymeric form. Granulates showed a significant improvement of in vitro drug dissolution behavior but the intragranular addition of crospovidone (PVP-CL) was found to be necessary to produce tablets with a satisfactory disintegration time and a remarkable increase of the drug dissolution rate [22].

Granules of griseofulvin (2.5, 5.0%) were prepared by melt granulation technique using PEG 3350 and Gelucire 44/14 both in 20% concentration as a melt binder and transferred into hard gelatin capsules. Dissolution rate of all prepared granules was higher as compared to pure drug and its physical mixtures. Granules having PEG as binder showed large dissolution enhancement relative to both physical mixtures and drug alone while granules containing Gelucire 44/14 as binder showed a significant dissolution enhancement as compared to drug but slightly enhancement compared to physical mixtures. The increase in dissolution rate was ascribed to the highly polar environment provided by water-soluble carriers, part of the drug dissolved in the binder and formation of monotectic mixture of drug and PEG [23].

Compacts of naproxen, nifedipine, and carbamazepine at a 1:1 polymer:drug weight ratio were prepared using HPMC USP Type 2208 (K3LV), HPMC USP Type 2910 (E3LV and E5LV) and methyl cellulose polymers by slugging and roller compaction method. The roller compaction and slugging methods produced comparable rate and extent of drug dissolution. This method require no solvent or heat for formulation and is cost effective, quicker, readily scalable at industrial scale [24].
Micronized danazol powders were prepared by ultra rapid freezing using polyvinylpyrrolidone K-15 at a 1:2 ratio and 0.55% total solid in either tert-butanol heated to 313 K or acetonitrile solvent at room temperature with enhanced dissolution of danazol. Use of different solvents markedly alters surface morphology of powder. Danazol powder produced by acetonitrile were spherical and uniform in size as a result of the more rapid and uniform cooling of the droplets relative to tert-butanol. This process is viable and robust for producing high surface area nanostructured powders for enhancing dissolution [25].

Coevaporates of prochlorperazine maleate (PCPM) were prepared by solvent evaporation method using hydroxypropyl methylcellulose phthalate as a carrier for solubilization of drug in alkaline medium and ethyl cellulose, hydroxypropyl cellulose for controlling the dissolution rates of weak basic drug PCPM. This method ensures maximum bioavailability with controlled release of drug from preparation [26].

Fast-dissolving mucoadhesive microparticles for sublingual administration could be a suitable alternative to fast-dissolving tablets because the sublingual absorption can be improved as a consequence of prolonging residence time on the mucosa and reducing the amount of swallowed drug. Low-swellable mucoadhesive methacrylic copolymers, namely viz. Eudragit® L sodium salt and Eudragit® S sodium salt, were used as effective carriers for the preparation of the microparticles in ratio ranging from 15/85 to 85/15% (m/m) by spray drying. Their intrinsic dissolution rates are faster than those of most commonly used mucoadhesive polymers. Piroxicam was present in amorphous form in all the prepared microparticles which was anticipated due to H-bond between the NH group of piroxicam and a CO group of the copolymers. The best delivery system made of piroxicam and Eudragit® L sodium salt in the ratio 70/30% (m/m) was able to increase the apparent drug solubility by two times while maintaining the desirable mucoadhesive properties [39].

**Superdisintegrants**

Dissolution of poorly water soluble drugs can be markedly improved by use of superdisintegrants like sodium starch glycolate, croscarmellose sodium, crospovidone, crosslinked polyvinylpyrrolidone, crosslinked alginic acid etc [40]. Some of the recent studies utilizing superdisintegrants are presented in Table 3.

Sodium starch glycolate swells 7- to 12-fold in less than 30 sec. uniformly in all three dimensions while croscarmellose swells 4- to 8-fold in less than 10 sec. in two dimensions leaving fibre length similar. This indicates that rate, force, and extent of swelling have an important role in disintegrants that work by swelling. Cross-linked PVP swells little (due to absence of cationogenic groups in the molecule) but returns to its original boundaries quickly after compression. Wicking or capillary action also is postulated to be a major factor in the ability of cross-linked PVP to work as superdisintegrant [41]. Gellan gum and xanthan gum also have extensive swelling properties for faster disintegration. Calcium silicate is a highly porous superdisintegrant which acts by wicking action. Cross-linked alginic acid is a hydrophilic colloidal substance with high sorption capacity and acts by swelling or wicking action [40].

Carrier particles of size from 50 to 1000 microns with cross-linked sodium (Ac-Di-Sol) disintegrant in an optimum amount of 5 to 10% weight were prepared by granulating liquid (ethanol) which did not dissolved the disintegrant or caused the disintegrant to swell [42]. These carrier particles were mixed with micronized oxazepam for 50 hours to obtain ordered mixture with surface area ratios of 0.08, 0.57 and 1.5. With addition of 1% sodium lauryl sulphate in finely dispersed form in mixture with the pharmaceutical substance in the carrier, the dissolution rate
### Table 3: Superdisintegrants and techniques employed for enhancing dissolution of poorly water soluble drugs

<table>
<thead>
<tr>
<th>S/N</th>
<th>Drug</th>
<th>Superdisintegrant</th>
<th>Technique</th>
<th>Mechanism of Dissolution Enhancement</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Naproxen</td>
<td>Cross-linked polyvinylpyrrolidone</td>
<td>Drug loading on the surface of a carrier</td>
<td>Higher surface area of the carrier and capillary action of carrier</td>
<td>(51)</td>
</tr>
<tr>
<td>2.</td>
<td>Methyprednisolone, Phenylbutazone</td>
<td>Sodium starch glycolate</td>
<td>Wet granulation</td>
<td>Swelling action of carrier</td>
<td>(44)</td>
</tr>
<tr>
<td>3.</td>
<td>Nifedipine</td>
<td>Croscarmellose sodium and Crospovidone</td>
<td>Physical mixtures</td>
<td>Swelling action of croscarmellose sodium and capillary action of crospovidone</td>
<td>(44)</td>
</tr>
<tr>
<td>4.</td>
<td>Oxazepam</td>
<td>Cross-linked sodium (Ac-Di-Sol)</td>
<td>Ordered mixing</td>
<td>Swelling action of carrier</td>
<td>(44)</td>
</tr>
<tr>
<td>5.</td>
<td>Furosemide</td>
<td>Crospovidone</td>
<td>Formation of coprecipitates by solvent method</td>
<td>Capillary action of carrier</td>
<td>(45)</td>
</tr>
<tr>
<td>6.</td>
<td>Flurbiprofen</td>
<td>Sodium starch glycolate (Primogel)</td>
<td>Dispersible tablets by wet granulation</td>
<td>Swelling action of carrier</td>
<td>(46)</td>
</tr>
<tr>
<td>7.</td>
<td>Tenoxicam</td>
<td>Primogel, Ac-Di-Sol, and Kollidon CL</td>
<td>Coprecipitation/Solvent evaporation method</td>
<td>Swelling action of sodium starch glycolate, croscarmellose sodium and capillary action of crospovidone</td>
<td>(47)</td>
</tr>
<tr>
<td>8.</td>
<td>Amorphous Ibuprofen</td>
<td>Cross-linked polyvinylpyrrolidone</td>
<td>Solvent deposition</td>
<td>Faster dissolution from amorphous ibuprofen, drug deposition on carrier surfaces and polymer swelling</td>
<td>(48)</td>
</tr>
<tr>
<td>9.</td>
<td>Aspirin</td>
<td>Sodium starch glycolate, Croscarmellose sodium, Crospovidone</td>
<td>Direct compression</td>
<td>Swelling action of sodium starch glycolate, croscarmellose sodium and capillary action of crospovidone</td>
<td>(49)</td>
</tr>
<tr>
<td>10.</td>
<td>Hydrochlorothiazide</td>
<td>Sodium starch glycolate, Croscarmellose sodium</td>
<td>Direct compression</td>
<td>Swelling action of carriers</td>
<td>(49)</td>
</tr>
<tr>
<td>11.</td>
<td>Carbamazepine, Nifedipine</td>
<td>Cross-linked polyvinylpyrrolidone (Kollidon CL-M)</td>
<td>By adsorption of drugs onto high surface area carriers</td>
<td>Capillary action of carrier</td>
<td>(30)</td>
</tr>
<tr>
<td>12.</td>
<td>Chloroquine phosphate</td>
<td>Sodium starch glycolate, Croscarmellose sodium and Crospovidone</td>
<td>Wet granulation</td>
<td>Swelling action of sodium starch glycolate, croscarmellose sodium and capillary action of crospovidone</td>
<td>(52)</td>
</tr>
</tbody>
</table>
was independent of whether or not the water solvent contains an additional surfactant [43] and the dissolution rate increased so markedly that about 90% of the composition has passed into solution after two minutes.

Improvement of dissolution rate of nifedipine by solid deposition on high percentages of sodium starch glycolate and croscarmellose sodium respectively, was explained by deagglomeration of the micronized drug by the superdisintegrant particles and solid deposition upon the surface of strongly swelling superdisintegrants which act as a carrier. As an effect of swelling of the superdisintegrants, the 'wetted' surface of the carrier increases, this promotes wettability and dispersibility of the particulate system [44].

Coprecipitates of furosemide-crospovidone were prepared by solvent method using methanol with enhanced dissolution rate due to association between the functional group of furosemide and crospovidone at the molecular level. The association was probably between imino and sulfonylamide group of furosemide and carboxyl group of crospovidone [45].

Dispersible tablets of flurbiprofen were formulated using pregelatinised starch, microcrystalline cellulose and sodium starch glycolate disintegrants alone and in different combinations containing different concentrations of disintegrants by wet granulation method by employing starch paste as binder. Among all, tablets formulated by employing sodium starch glycolate disintegrated rapidly and gave faster dissolution of flurbiprofen [46].

Coprecipitates of tenoxicam with sodium starch glycolate (Primogel), Ac-Di-Sol, and cross-linked PVP (Kollidon CL) were prepared by solvent evaporation method with enhanced dissolution of tenoxicam. Kollidon CL was found to be most effective disintegrant of the three evaluated, especially at 1:9 ratios [47].

Drug/carrier systems of amorphous ibuprofen and cross-linked polyvinylpyrrolidone were prepared as physical mixes, and drug was loaded onto the polymer by hot mix and solvent deposition method. Increased dissolution rate of ibuprofen were achieved in the descending order of solvent deposition, hot mixes, physical mixes. The increased dissolution rate could be ascribed to a combination of faster dissolution from amorphous ibuprofen, drug deposition on carrier surfaces and polymer swelling [48].

Tables of aspirin were prepared by direct compression technique using sodium starch glycolate, croscarmellose sodium, crospovidone as superdisintegrants. It was found that the disintegration time was comparable for tablets formulated with 1% croscarmellose sodium, 2% crospovidone, or 5% sodium starch glycolate. However the dissolution of aspirin from these tablets varied in the following descending order despite the closeness of their disintegration times: croscarmellose sodium, sodium starch glycolate, crospovidone [49]. Similarly hydrochlorothiazide tablets were prepared by direct compression method using sodium starch glycolate, croscarmellose sodium as superdisintegrants with enhanced dissolution [50].

Carbamazepine and nifedipine were dissolved in methanol, polyethylene glycol, 2-pyrrolidone and adsorbed onto the surface of cross-linked polyvinylpyrrolidone (Kallidone). The solvent binding capacities decreased in the order of methanol, PEG 4000, 2-pyrrolidone. Improved dissolution rate of drugs was observed due to high surface area of the carrier [30]. Similarly increase in dissolution rate of naproxen by loading on surface of cross-linked polyvinylpyrrolidone was observed [51].

Tables of chloroquine phosphate using sodium starch glycolate, croscarmellose sodium, and crospovidone as disintegrants in 2% w/w concentration were prepared by wet granulation technique using intragranular and extragranular methods. Disintegration
and dissolution studies revealed intragranular method of application of disintegrants more suitable which help the tablet to burst into smaller particles as well as it may help to dissolve the drug faster. Croscarmellose sodium incorporated intragranular method gave better results than extragranular method as well as better than sodium starch glycolate and crospovidone incorporated extragranular and intragranular methods for the chloroquine phosphate [52].

All above formulations prepared using superdisintegrant indicates that use of superdisintegrants is an easy alternate to enhance dissolution of poorly water soluble drugs without the addition of any other excipient and changing the methodology of preparation of specific drug. The only disadvantage associated with the use of superdisintegrants is its cost but overall cost of formulation is less as compared to opting specific measure to enhance dissolution.

**Surfactants**

Various surfactants like Polyglycolized glyceride (Labrasol), Tweens, Spans, Polyoxyethylene stearates and synthetic block copolymers like Poly (propylene oxide)-poly (ethylene oxide) – poly (propylene oxide), an example of poloxamers based micelles, Poly (beta-benzyl-L-aspartate) -b- poly (ethylene oxide), Poly (caprolactone) -b- poly (ethylene oxide) etc are used as carrier for dissolution enhancement (Table 4). Improvement of drug solubility by using the amphiphilic surfactants is due to lowering surface tension between drug and solvent, improvement of wetting characteristics and micellar solubilization of the drugs. Micelles are supramolecular self assemblies of macromolecules where unimers are held by non-covalent interactions. The core of the micelles solubilizes drugs whereas the corona/shell allows for their suspension in aqueous media [1].

Solid dispersions of albendazole using poloxamer 407 as surfactant at 1:1, 1:3, 1:5 weight ratio were prepared and results revealed a requirement of 0.75% as minimum concentration of poloxamer for solubility enhancement due to surface active property and critical micellar concentration. The albendazole-poloxamer melt (1:5 ratio) showed 16.1 fold dissolution rate and 9.4 fold in dissolution efficiency as compared to that of pure drug due to solubilization effect in the diffusion layer [37].

Solid dispersions of rofecoxib were prepared by hot-melt method using poloxamers (Lutrol® F127 and Lutrol® F68) in 50%, 75% and 90% w/w proportion. Enhancement in solubility of system was observed due to micellar solubilization and/or reduction of activity coefficient of the drug through reduction of hydrophobic interaction(s) and higher dissolution was observed at high (90%) carrier concentration [2].

Several liquisolid compacts were prepared by dispersing piroxicam in tween 80 as liquid to prepare liquid medication of the different drug concentrations with different ratios of drug:tween 80 ranging from 1:1 to 1:9 using binary mixture of microcrystalline cellulose (carrier powder)-silica (coating material) and finally compressing. Results revealed enhanced dissolution rate because drug is already in solution in tween 80 and same time drug is carried by powder particles of the liquisolid vehicle. Thus, its release is accelerated due to increased wettability and surface availability to the dissolution medium [31].

**Conclusion**

Numerous technological advancements have been introduced for dissolution enhancement of poorly water soluble drugs. Most of these
techniques utilize inert carriers which improve the drug’s physicochemical properties like solubility, particle size, crystal habit etc. Some of the carriers are especially capable of forming highly water soluble amorphous forms when the drugs are dispersed in them or by size reduction (co-micronization). Complexation of drug with suitable carrier also alters the solubility and dissolution characteristics due to extremely high aqueous solubility of the carrier. The solubility and dissolution rate improvements are also expected due to co-solvency effect and solubilisation effect of carriers in aqueous vehicles. In a nutshell it could be said that carrier induced physical modifications are an important tool to a formulation scientist in designing immediate and fast release drug delivery systems. The article continues as Part II [Int J Health Res, Sept 2009; 2(3)] which describes applications of cyclodextrins, carbohydrates, hydrotropes, polyglycolized glycerides, dendrimers, acids and other carriers in enhancing dissolution of drugs.

References

43. Nystrom C, Westerberg M. A pharmaceutical composition for rapid release of the active component comprising an ordered mixture and a surfactant. WO 90/04962 to Kabivitrum AB, Stockholm (SE).
47. Aly AM, Semreen M, Qato MK. Superdisintegrants for solid dispersion To produce rapidly disintegrating tenoxicam tablets via camphor sublimation. Pharm Tech 2005;68-78.