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An Update on Some Recent Solubility Enhancers as Pharmaceutical Excipients

VIVEK PURI, PRATIMA SHARMA AND MANJU NAGPAL*

Chitkara College of Pharmacy, Chitkara University, Punjab, India

***Email: nagpalmanju@ymail.com**

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Abstract At present the pharmaceutical academia and industries are focusing on the use of natural materials and resources for development of pharmaceutical product. Due to advances in drug delivery technology, currently, excipients are included in novel dosage forms to fulfill specific functions. Various natural polymers are widely being studied as a potential carrier material for site specific drug delivery because of its non-toxic and biocompatible in nature. Natural polymers (polysaccharides) have been investigated for drug delivery applications as well as in biomedical fields**.** Modified polymer or synthetic polymers have found its application as a support material for cell culture, tissue engineering and gene delivery. Recent trends towards use of natural products or plant based products demand the replacement of synthetic additives with natural ones. These natural materials have many advantages over synthetic ones as they are biodegradable, chemically inert, less expensive, nontoxic and widely available. This review provides an overview of the different modified polymer derivatives and their applications with special consideration being put on biomedical engineering and controlled drug delivery.

Keywords: Soluplus, captisol, gum, polymer, biodegradable, synthetic

1. INTRODUCTION

In recent years, polymers those are derived from plant origin have evoked tremendous interest because of their diverse pharmaceutical applications such as diluent, disintegrant, binder in tablets; thickeners in oral liquids; protective colloids in suspensions; binder and gelling agents in gels; and bases in suppository. They are also used in textiles, cosmetics, paints and paper making and other products. (11).

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These natural gums and mucilages are preferred over the synthetic ones because they are cheap, biocompatible, nontoxic, chemically inert, soothing action, availability, nonirritant nature of the excipients and easily available than the synthetic ones. Demand for these substances is increasing and new sources are being developed. Carbohydrate polymers are widely used in recent years in pharmaceutical applications and biomedical due to their biodegradability and biocompatibility. The polysaccharides stand for one of the most abundant industrial raw materials and have been the subject of intensive research due to their sustainability, bio-safety and bio degradability**.** The natural gums are product obtained as a result of metabolic mechanisms of plants. These gums are either water soluble or absorb water to form a viscous solution. Natural gums are easily available, economic and found useful as tablet binder. For example neem gum, khaya gum, mango gum etc. Neem (*A. Indica, A. Juss*) is perhaps the most useful and very beneficial traditional medicinal plant in India. Gum is obtained from the incised trunks of local *A. Indica* plant (belongs to family Meliaceae). Khaya gum is obtained from incised trunk of *K. grandifolia* (belongs to family Meliaceae). The mango tree (*M. Indica*, Family: Anacardiaceae)is also natural polymer which is used in pharmaceutical applications. Each and every part of the tree (bark, leaves, root, kernel, seed and fruit) serves a certain purpose, such as diuretic, astringent, aphthous, stomatitis, diabetes, scabies, asthma, urethritis, dysentery and other parasitic skin diseases. Hupu gum is the dried gummy exudate obtained from the deciduous tree of *C. religiosum*, (family Cochlospermaceae). These gums have been shown to possess binding properties. Synthetic polymers such as Captisol is derivative of anionic -cyclodextrin with a sodium sulfonate salt separated from the hydrophobic cavity by a butyl ether spacer group, which is used as polymer for the improving bioavailability, solubility and stability of the drugs. Soluplusis a polyethylene glycol, polyvinyl acetate and polyvinylcaprolactam based graft copolymer. It is a novel excipient which is used as a carrier matrix and solublizers. Soluplus shows excellent solubilizing properties for BCS class II drugs. (23).

2. NATURAL EXCIPIENTS

2.1 Neem Gum

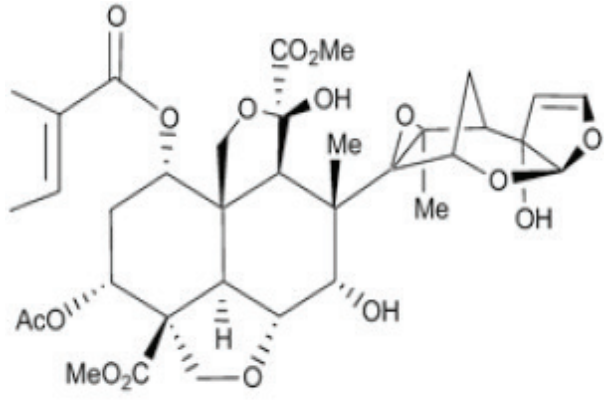
Neem (*A. Indica, A. Juss*) is perhaps the most useful and very beneficial traditional medicinal plant in India. (19). Innumerable part of the neem tree(gum, roots, flower, leaf etc.) has some medicinal property and is thus

commercially credulous. This is well known in India for more than 2000 years having a wide spectrum of biological activity.

2.1.1 Gum Extraction

The Neem gum is collected then hydrated in a sufficient amount of distilled water with sporadic stirring and irrelevant materials were removed by filtering using a Buchner funnel under negative pressure. The gum is precipitated with 95% ethanol from the filtered slurry; the precipitated gum is then filtered, washed with acetone for several times and dried in a hot air oven at 30°C for 96 h before milling and sieving with a mesh No. 60 (250 μm) and then dried fine powder is formed and stored in an amber colored bottle until needed.(1).

2.1.2 Chemical Structure of Neem Gum



24 Azadirachtin

Figure 1: Structure of neem active constituents.

2.1.3 Biological Activities of Various Part of Neem

Large number of compounds has been isolated from various part of neem; a few of them have been studied for biological activity (Table 1). For examples:

2.1.4 Medicinal Uses of Various Part of Neem

2.1.5 Other Uses of Neem

(i) Antifungal activity: The leaves contain nimbidol and edunin, which have antifungal properties. According to The Neem Foundation, compounds

Table 1: Various compounds from various parts of Neem plant and their biological activity.

S.No.	Compounds	Source	Biological Activity
1	Nimbin	Seed Oil	Spermicidal
2	Nimbidine	Seed Oil	Antifungal, Antibacterial, Anti-inflammatory, Antipyretic, Antiarthritic, Hypoglyceamic, Spermecidal, Diuretic
3	Azadirachtin	Seed Oil	Antimalarial
4	Cyclic Tetrasulphide	Leaf	Antifungal
5	Mahmoodin	Seed Oil	Antibacterial
6	Margolone	Bark	Antibacterial
7	Gallic acid & Catechin	Bark	Anti-inflammatory, Immunomodulatory
8	PolysaccrideG1A, G1B	Bark	Antitumour
9	Nimbolide	Seed Oil	Antibacterial, Antimalarial
10	Gedunin	Seed Oil	Antimalarial, Antifungal
11.	NB-2 Peptidoglucan	Bark	Immunomodulatory

Table 2: Enlisted medicinal uses of various parts of Neem Plant.

S.No	**Parts**	**Medicinal Uses**
1.	Flower	Elimination of intestinal worms and phlegm, bile suppression
2.	Fruit	Urinary disorder, wounds and leprosy, relieves piles, intestinal worms, diabetes
3.	Seed Pulp	Intestinal worms and leprosy
4.	Gum	Scabies, wounds, ulcers, effective against skin disease like ringworms
5.	Leaf	Leprosy, epistaxis, intestinal worms, eye problems, anorexia, skin ulcers, bioliosness
6.	Bark	Analgesic, antipyretic
7.	Twing	Asthma, piles, phantom tumour, diabetes, spermatorrhoea, relieves cough, intestinal worms
8.	Oil	Intestinal worms & leprosy
9.	Root, Bark, Flower and Fruits	Billiary, burning sensation, skin ulcer, blood morbidity

in the leaves are perilous to fungus. By inhibiting the growth of Tinea rubrum, Nimbidin also demonstrated anti fungal activity.

(ii) Antibacterial activity: Nimbidin can completely inhibit the growth of *Mycobacterium tuberculosis* thereby showed bactericidal activity. The neem oil along with the leaves reveal antibacterial and antiseptic benefits. The paste form of neem leaves are mostly used to treat manydifferent skin conditions for example, eczema, rashes, psoriasis and acne.

(iii) Antiviral activity: Aqueous extracts from the leaves has shown antiviral properties and offers antiviral activity against vaccinia virus, and measles virus *in vitro.*

(iv) Antimalarial activity: Seeds and leaves extracts are effective against both chloroquin-resistant and sensitive strain malarial parasites. Nimbolideinhibits the Plasmodium falciparm which illustrate antimalarial activity.

(v) Reproductive health: Neem reduces fertility in both men and women without affecting sexual performance or libido. Neem is also used as a vaginal suppository because of spermicide properties and could prevent sexually transmitted infections.

(vi) Arthritis: Nimbin is an anti-inflammatory that is the main reason of using neem to cure arthritis. Polysaccharides present in the neem, reduces the inflammation and pain.

(vii) Skin health: Neem also removes the little parasites that cause scabies. According to ayurveda practice, neem oil is used topically as a therapy for psoriasis and eczema.

(viii) Some other uses of neem gum such as antifertility, antitumour, antiglyceamic etc. (23).

2.1.6 Pharmaceutical Applications of Neem gum

(i) Suspending agent, Thickening agent, Adhesive agent, Sustained release agent

(ii) Binding agent (binder in tablets): Various synthetic, semi-synthetic and natural substances such as celluloses, starches, and gums have been employed in pharmaceutical tablet formulations as binders. Gum is an example of hydrophilic substance employed in pharmaceutical solid dosage forms mainly as binders and directly compressible excipients. A research report assessed the activity of neem gum as a binder in a paracetamol tablet dosage form. Inclusion of neem gum improved the balance between binding and disintegration properties of paracetamol tablets produced than those containing ACA. (1).

(iii) Coating agent: Neem gum did not affect the drug release from the coated and the mechanical properties tablet adversely. The% LOD and coating uniformity of neem gum coated tablets ensured good finish. Neem gum is accomplished natural, cheap, biodegradable and ecofriendly film former for aqueous filmcoating of tablets, moisture sensitive drug or particularly for bitter taste. (15).

2.4 MANGO GUM

Mango gum is a dried gummy exudate polysaccharide obtained from the bark of *M. indica*, (family Anacardiaceae) [Madhuri *et al*. (2014)]. Mangiferin, being a polyphenolic antioxidant and a glucosyl xanthone, has strong immunomodulation, hypotensive, antioxidant, anti-lipid peroxidation, cardiotonic, wound healing, antidegenerative and antidiabetic activities. Ripe mango fruit is considered to be stimulating and freshening. The juice is used in heat stroke and recuperative tonic. The seeds are used as an astringent and in the treatment of asthma. Fumes from the burning leaves are inhaled which gives relief from infections of the throat and hiccups (27, 18). The bark is used as astringent and also used in diphtheria and rheumatism, and it is believed to possess a tonic action on mucus membrane. The gum is used for scabiesand dressings for cracked feet. Most parts of the mango tree are used for medicinal purpose and the bark also contains tannins, which are used for the purpose of dyeing (25).

2.2.1 Purification of Mango Gum from Mango Tree

The mango gum was dried and hydrated in distilled water for one day with continuous stirring; irrelevant materials were removed by straining through muslin cloth. The gum was precipitated with 95% ethanol from the filtered slurry; the precipitated gum was then filtered and dried on water bath at 50°C. The dried gum was milled using a laboratory blender and stored in tightly closed container (27, 18).

2.2.2 Chemical Nature of Mango or Mango Gum

Mangiferin contains xanthone glycoside major bio-active constituent, tannins, isomangiferin & gallic acid derivatives. Gums and mucilages are polysaccharides and they contain sugars. The bark is reported to contain protocatechic acid, γ-aminobutyric acid, mangiferin, catechin, alanine, glycine, kinic acid, shikmic acid and the tetracyclic triterpenoids. Indicoside A and B, manghopanal, manglupenone, mangocoumarin, mangoleanone, cycloartan-3β-30-diol and derivatives, mangsterol and mangiferolic acid methyl ester and others have been isolated from stem bark of mango. Root of mango contains

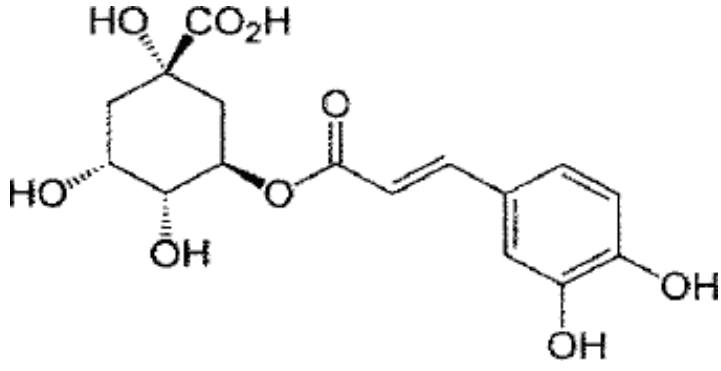


Figure 2: Mango gum (chemical nature).

the chromones, 3-methoxy-2-(4'-methyl benzoyl)-chromone and 3-hydroxy-2-(4'-methylbenzoyl)-chromone and the leaf and flower yield an essential oil containing humulene and elemene. The fruit pulp contains vitamins A and C, xanthophylls, β-carotene.

2.2.3 Pharmaceutical Uses of Mango Gum

Mango gum resin is collected from the incised trunk of *M. indica*. Various parts of plant are used as a dentrifrice, tonic, astringent, diaphoretic, stomachic, antiseptic, laxative and diuretic and to treat diarrhea, anaemia, asthma, bronchitis, cough, hypertension, insomnia, toothache, leucorrhoea, haemorrhage and piles. All parts are used to treat abscesses, tumour, broken horn, rabid dog or jackal bite, datura poisoning, snakebite, stings, heat stroke, miscarriage, anthrax, blisters, wounds in the mouth, glossitis, indigestion, bacillosis, bloody dysentery, liver disorders, excessive urination, tetanus and asthma (27).

2.2.4 Applications of Mango or Mango Gum

(i) **Anti-diabetic:** A 50% ethanolic extract of the leaves produced hypoglycemic effect at a dose of 250 mg/kg. The effect of the aqueous extract of the leaves of *M. indica* on blood glucose level in glucose - induced hyperglycaemic, normoglycaemic, and streptozotocin (STZ)-induced diabetic rats has been assessed. The results showed the aqueous extract of the leaves of MI possess hypoglycaemic activity.

(ii) **Antiviral activity**: *In vitro studies* give against *Herpes simplex* virus type 2; it inhibits the late event in HSV-2 replication. But it does not directly inactivate HSV-2. *In vitro* mangiferin also inhibit HSV-1 virus replication within.

(iii) **Anthelmintic and anti-allergenic activity:** The study of mangiferin isolated from extract of *M. indica* was carried out to find out anti-allergic properties. This natural extract of *M. indica* could be successfully used in the treatment of allergic disorders.

(iv) **Antiparasitic activity:**In a neonatal mouse model, mangiferin showed similar inhibitory activity at 100 mg/kg *Cryptosporidium parvum* than the same dose (100 mg/kg) of an active drug (paromomycin).

(v) **Antibone resorption:** Four water extracts of *Kampo* formulae were screened for their inhibitory effect on bone resorption induced by parathyroid hormone in organ culture of neonatal mouse parietal bones. Mangiferin isolated and tested *in vitro* showed a significant inhibitory effect on this model.

(vi) **Anti-tumor-anti-HIV:** Significant cytotoxic activities have been established by the stem bark extract of mango against the breast cancer cell as well as against a colon cancer cell and a renal cancer cell line. *In vitro*, Mangiferin dose- and time-dependently inhibited the proliferation of K562 leukemia cells and induced apoptosis in K563 cells line. These results recommend that mangiferin has a potential as a naturally-occurring chemopreventive agent.

(vii) **Antispasmodial and antipyretic activity:** The stem bark extract was evaluated for antiplasmodial activity against *Plasmodium yoelii nigeriensis* and antipyretic activity. A reduction in yeast-induced hyperpyrexia was also produced by the extract of *M. indica*.

(viii) **Immunomodulatory**: Immunomodulatory activity of alcoholic extract of stem bark of *M. indica* was investigated in mice models. Mangiferin mediates the down-regulation of NF-*x*B, suppresses NF-*x*B activation induced by inflammatory agents, increases the intracellular glutathione (GSH) levels, including tumor nuclear factor (TNF) and potentiates chemotherapeutic agent-mediated cell death; this suggests a possible role in combination therapy for cancer.

(ix) **Anti-diarrhoeal:** The potential anti-diarrhoeal activity of methanolic and aqueous extracts of seeds of MI has been evaluated which was induced by castor oil and magnesium sulphate in mice models and results demonstrate that the extracts of MI have significant anti-diarrhoeal activity and part of the activity may be attributed to its effect on intestinal transit.

(x) **Anti-bacterial and antifungal activity:** *In vitro* agar diffusion technique in mangiferin showed activity against 7 bacterial species, *Salmonella agona, Bacillus pumilus, B. cereus, Staphylococcus aureus, S. citreus, Klebsiella pneumoniae*, 1 yeast (*Saccharomyces cerevisiae*),

Escherichia coli and 4 fungi (*Thermoascus aurantiacus, Trichoderma reesei, Aspergillus flavus* and *A. fumigatus*).

2.3 Hupu Gum

Hupu gum is the dried gummy exudate obtained from the deciduous tree of "*Cochlospermum religiosum*, Alston" (synonym Cochlospermum gossypium), (family Cochlospermaceae). Hupu gum tree is abundantly found in forests and hills of Chittoor. Its applicability is reported for industries like paper, nicotine sprays, printing gum and in the preparations of lotions and pastes. Some investigation have been conducted on hupu gum as a potential food additive in food &nutria-tion industries. Basically it is a polymer of rhamnose, glucuronic acid, galacturonic acid, b-D galactopyranose, b-D-glucose, galactose, a-D-glucose arabinose, fructose and mannose with sugar linkage. The enhancement of dissolution profile of Pioglitazone HCl using modified Hupu gum as carriers by solid dispersion technique. It is reported that the swelling ability of the hupu gum improves dissolution rate of poorly water soluble drug (26, 24).

2.3.1 Chemical Nature of Hupu Gum

Hupu gum is a naturally occurring polysaccharide derived as an exudate from the tree. Hupu gum is a polymer of galacturonic acid, b-D galactopyranose, rhamnose, a-D arabinose, mannose and fructose with sugar linkage. Modified hupu gum were characterized for swelling index, viscosity and water retention capacity. The modified hupu gum gives tremendous changes in structural bonding, crystallinity, cohesive and adhesive forces of attraction of drug, at different temperature, which help to lower the viscosity and swelling index and this reacts to increases water holding capacity which improves the wettability of drug and helps to dissolve the poorly water soluble drug (24).

2.3.2 Preparation of Modified Hupu Gum

Powdered hupu gum is placed in a porcelain bowl and subjected to heating in hot air oven for 140°C for 2 h. The prepared modified hupu gum is finally resieved (100 mesh) and stored in airtight container at 25°C. (24)

2.3.3 Application of Hupu Gum

a. **To Enhance the Solubility of Drug** Solid dispersion was prepared by co-grinding method using hupu gum and modifiesd hupu gum with pioglitazone HCl. The solubility of Pioglitazone HCl increases with hupu gum and significantly high with modified hupu gum. Hupu gum resulted in formation of lumps of drug-carrier particles during

dissolution, whereas pioglitazone HCl-modified hupu gum particles dispersed rapidly. Hupu gum increases water holding capacity which improves the wettability of drug and helps to dissolve poorly water soluble drug (24).

b. Target Drug Delivery System: Hupu gum has been used as the drug delivery carrier. Solid dispersions of mefanimic acid with hupu gum were prepared by kneading method at different ratios. Hupu gum (HG) was used as plug. The solid dispersions have been used for the formulation of pulsin caps. Solid dispersions of mefenamic acid were filled in the bodies which were made insoluble by formaldehyde treatment. Sealing of body and cap were done using ethyl cellulose. Ethyl cellulose coating was employed to ensure the colon targeting of pulsin caps. The studies have clearly indicated that formulations were very effective to deliver the drug specifically to colon. (5).

c. To Enhance Mucoadhesive Property: The study was undertaken to assess the mucoadhesive property of hupu gum in design of mucoadhesive buccal patches using Propanolol Hcl as a model drug. Mucoadhesive strength measurement was conducted for formulation containing hupu gum with drug and show it good mucoadhesive property. (12).

3. SYNTHETIC EXCIPIETNS

3.1 Captisol

Captisol® is a patent protected, unique modified cyclodextrin, whose chemical structure was rationally designed to enable the creation of new products by significantly improving bioavailability, solubility, stability and dosing of active pharmaceutical ingredients (APIs). CAPTISOL is a derivative of anionic-cyclodextrin with a sodium sulfonate salt separated from the hydrophobic cavity by a butyl ether spacer group. (30).

3.1.1 Chemical Nature of Captisol

Captisol is the trade name for modified cyclodextrin preparation. Scientists of the 'Kansas University'invented and initially developed the Captisol. Captisolis a combination of polyanionic-cyclodextrin derivatives of a sodium sulfonate salt tethered to the lipophilic cavity by sulfobutyl ether (SBE) or a butyl ether group. The selection of Captisol was based upon evaluations of the mono, tetra and hepta-substituted preparations such as the cyclodextrin preparation with the most desirable safety profile and drug association properties (30).

3.1.2 Structure of Captisol: ***Structure of Captisol and site of action is shown in figure 3 and 4.***

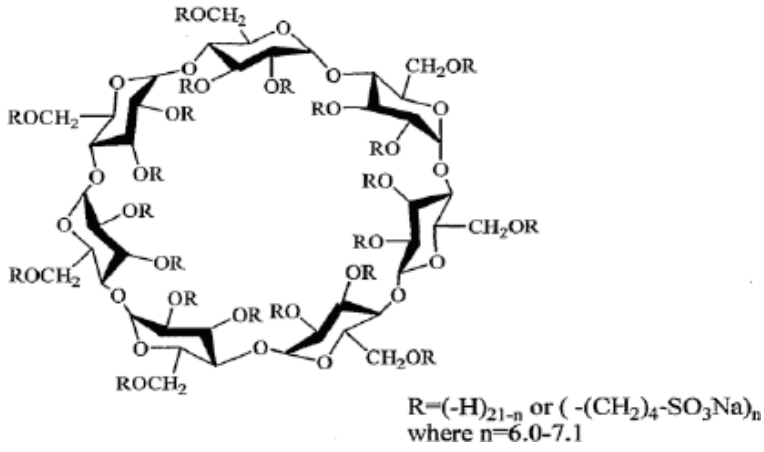


Figure 3: Structure of CaptisolFigure 4: Site of action.

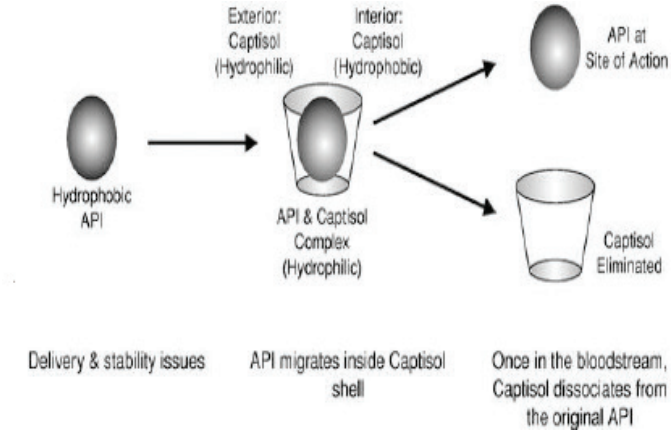


Figure 4: Site of action.

3.1.3 Benefits of Captisol

(i) Product Development: Product development is a composite process for discovery and evaluation to develop and commercialize CAPTISOL provides an elegant solution to stability and solubility hurdles faced during each phase of the development process.

(ii) Solubilizer: Neutral, anionic and cationic drugs as well as small and large molecules, have been effectively complexed by Captisol. Aqueous

solubility was increased by a factor of 10 to 25,000 depending drug upon the compound. In comparison to other solubilization technologies, product or traditional formulation system, the solubility and feasibility effectiveness of Captisol can be rapidly assessed with a few simple lab experiments.

(iii) Stabilizer: Captisol provides protected environment for the drug molecule in its lipophilic cavity while its hydrophilic surface provides good water solubility and stability. Interaction of the drug with CAPTISOL can reduce drug decomposition in the aqueous environment by protecting the labile region from the potential reactants.(10).

3.1.4 Applications of Captisol

a. Enhances drug solubility: Dissolution enhancement of antiepileptic drug carbamazepine was improved by forming inclusion complex using Captisol. The inclusion complex exhibited significantly higher in vitro dissolution profile as compared with pure carbamazepine powder.

b. Enhances the drug stability: In aqueous solution stability of drugs can markedly improve on complexation with CAPTISOL. Enclosure of the drug in the cyclodextrin cavity can serve to reduce the rate of decomposition by 'hiding' the reactive center. CAPTISOL minimize aggregation, preventing adsorption to containers and refolding which helps in stabilizing some protein and peptide formulations. Captisol decrease the aggregation of insulin and increase the bioavailability to 96%. It can also help to improve the physical stability.

c. Effective Drug Delivery: Captisol may be applied in drug delivery in many ways. Pharmacokinetic results showed that drugs dissociate rapidly and quantitatively from their cyclodextrin complexes on dilution with tissue fluids. Chemical structure of Captisol was designed to maximize the safety of the material by minimizing the damaging effects produced by the parent cyclodextrin. Increased solubility and stability translate into enhancement of efficacy via increased dissolution rate or solubility in the lower GI, leading to greater and faster absorption, bioavailability and more rapid onset of action.

d. Safe Drug Carrier: Chemical structure of Captisol was designed to take advantage of the safety of the material by minimizing the damaging effects produced by the parent cyclodextrin. Captisol mainly targets the multi-billion dollar solubility fragment of the global drug delivery market. Captisol with advanced safety and excellent drug carrier property, makes it the standard solubility solution. For example anionic Sulfobutylether group was introduced to take advantage of the kidney's ability to quickly

excrete ionic compounds, hence minimizing the contact time between the kidney cells and the cyclodextrin.

3.2 SOLUPLUS

Various new active pharmaceutical ingredients having lipophilic nature, suffer from low bioavailability due to their low aqueous solubility and dissolution. Various approaches have been used like micronization, solubilization, complexation with polymer, salt formation, use of prodrug etc. but all these approaches having some limitations. The solubility can be overcome by soluplus using as a solubility enhancer. (16). Soluplus**;** a polyethylene glycol, polyvinyl acetate and polyvinylcaprolactame-based graft copolymer (PVAc-PVCap- PEG), a new polymer with amphiphilic properties is the novel excipient which is used as a carrier matrix and solublizer. Soluplus shows excellent solubilizing properties for BCS class II substances (29). The dissolution of poorly soluble drugs in aqueous media can be highly improved by the use of solid solutions with soluplus. The various techniques can be used for soluplus are Spray drying method, Solvent evaporation, Melting method, preparation of physical mixtures. Soluplus is a novel polymer specially designed for the fourth generation solid solutions towards dissolution enhancement. (9).

3.2.1 Chemical Structure of Soluplus

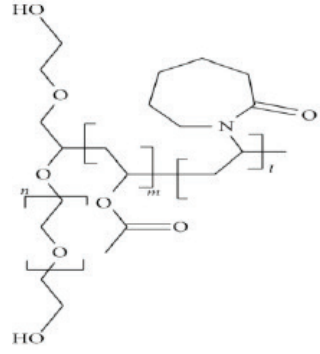


Figure 5: Structure of Soluplus.

3.2.2 Application

a. **Enhance Solubility:** The drug in presence of soluplus lead to improved wettability anddispersibility, as well as decrease in the crystalline state and increase of the amorphous fraction. Soluplus could be regarded as a carrier in solid dispersion systems in order to improve the dissolution

rate of poorly water soluble drugs. With its outstanding solubilisation properties, Soluplus is designed to specifically dissolve poorly soluble active pharmaceutical ingredients (APIs).

b. Excellent capability to form solid solutions: Soluplus exhibited superior performance in forming solid solutions, especially in hot melt extrusion processes. ME is an excellent technique for the preparation of solid dispersions as it has several advantages over other technique such as industrial feasibility, organic solvent free technology, high drug loading, less number of unit operations, anhydrous processing of moisture sensitive drug.

3.2.3 Methods Used with Soluplus

(i) Hot Melt Extrusion Method: The excellent extrudability and high flowability of Soluplus make it superior in hot melt extrusion. Soluplus shows advanced performance in forming solid solutions, especially in hot melt extrusion processes. Soluplus is not an adequate to solid solutions formed via hot melt-extrusion, but can be used as a matrix former in spray drying processes (6,13).

(ii) Solid Dispersion Method: The solid dispersion of various poorly water soluble drugs with Soluplus was prepared, such as soluplus and PEG 4000 was dissolved in methanol to which poorly water soluble drug was added with stirring, solvent was evaporated and the solid dispersion powder of drug and polymer was obtained (20).

(iii) Spray Drying Method: The dispersions were prepared by spray drying method. The spray drying was performed with various conditions such as inlet temperature, outlet temperature, and solution flow rate. The spray dried samples were stored in a desiccator. (8, 3).

(iv) Solvent Evaporation Method: The solid dispersion of various poorly water soluble drugs with Soluplus was prepared by solvent evaporation method. The drug and soluplus dissolved in solvent (methanol) and the solvent evaporated under pressure using the rotary evaporator and the residue dried under vacuum. (30).

3.2.4 Uses

a. Solubility Enhancer: Soluplus is an novel excipient that enables new levels of bioavailability and solubility for poorly soluble active ingredients. The polymer used in various different ways with different drugs to significantly improve solubility and bioavailability (20, 14).

Table 3: Research reports on various drugs using Soluplus as a carrier and the method used.

S.no.	Drug	Polymer	Preparation Technique	Temp (In-Out)
1.	Lafutidine	Soluplus	Hot melt extrusion	84
2.	Carbamazepine	Soluplus	Hot melt extrusion	150-180
3.	Carbamazepine	Soluplus, Eudragit	Hot melt Extrusion	165-185
4.	Itraconazol	Soluplus,	Freeze Dry Method	140-160
5.	Dronedaron HCL	Soluplus	Hot melt Extrusion	150
6.	Oxcarbazepine	Soluplus, Kollido -VA 64	Hot melt extrusion	180
7.	Artemethar	Soluplus, PEG400	Hot melt Extrusion	52-56
8.	Valsartan	Soluplus	Hot melt extrusion	115-120
9.	Atorvastatin Calcium	Soluplus	Spray drying	65-80 & 50-60
10.	Lovastatin	Soluplus	Hot melt extrusion	115-120
11.	Ezetimibe/ Simvastatin	Soluplus, Hydroxyp-ropyl-β-cyclodextrin	Hot melt extrusion	-

b. Binding Agent: The soluplus also used as a binding agent, due to this property the drug with soluplus can also be compressed into tablet. Its excellent ability to form solid solutions and outstanding solubilization capabilities, combined in one molecule, distinguish soluplus from other molecules that are used to form solid solutions. Soluplus is used as a binding agent in a wet granulation or a dry binder in direct compression.

c. Enhance Bioavailability: Soluplus can increase the bioavailability of poorly water soluble drugs. Solid solutions were prepared with Itraconazol with soluplus and fenofibrate with soluplus. The solid solution makes the active pharmaceutical ingredient (API) available in a dissolved state, the result showed improve bioavailability once in the body (5).

d. Spray Drying Agent: Soluplus is not limited to solid solutions formed via hot melt-extrusion, but can also be used as a matrix former in spray drying

processes. Soluplus can be used for spray drying of organic solutions. (9).

CONCLUSION

The low aqueous solubility of drug molecules is the limiting factor for their dissolution as well as bioavailability. Various novel excipients have been recognized, synthesized to overcome this problem. Now a days main research is on the development and identification of novel excipients whether natural or synthetic (Coprocessed, high functionality excipients). Current review has given a highlight about neem gum, hupu gum and mango gum; their use in formulation development as well as therapeutic benefits. Soluplus and captisol has also been discussed with their various benefits in drug product development of poorly aqueous soluble drugs. The gums and synthetic carriers has been explored as efficient solubility enhancers as evidenced with several researchers.

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