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Soluplus is a polymeric carrier which increased the solubility bioavailability, dissolution of various dosage form:- An overview.

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ABSTRACT
Soluplus®, a commercially available polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft copolymer, has emerged as a versatile polymer in pharmaceutical formulations due to its unique amphiphilic properties. This polymer possesses a hydrophilic polyethylene glycol fragment along with lipophilic vinylcaprolactam and vinyl acetate moieties, rendering It is appropriate for a variety of uses, especially improving the bioavailability, stability, and solubility of medications that are not very soluble in water. A lot of research has been done on Soluplus®'s ability to create solid dispersionswhere it serves as a stabilizer and a solubilizer, forming amorphous matrices that enhance dissolving rates and inhibit drug recrystallization. Moreover, Soluplus® has shown effective in a number of formulation processes, including solvent evaporation and hot melt extrusion, opening the door for the creation of cutting-edge drug delivery systems including nanoparticles and microparticles. This review emphasizes the benefits, uses, and characterization of and disadvantages of Soluplus® in pharmaceutical formulations, showcasing its potential to address formulation challenges and enhance drug delivery.

KEYWORDS: Soluplus, polyvinyl caprolactum-polyvinyl acetate-polyethelyne glycol, critical micelle concentration.

I. INTRODUCTION

The novel polymer Soluplus®, a copolymer of polyvinyl caprolactam, polyvinyl acetate, and polyethylene glycol, possesses amphiphilic characteristics due to the inclusion of a lipophilic vinylcaprolactam and VAc moiety inside its structure, together with a hydrophilic PEG fragment. created and intended for sturdy solutions. With its dual functionality as an active solubilizer via micelle production in water and a matrix polymer for solid solutions, Soluplus® can be regarded as a member of the fourth generation of solid dispersions, in contrast to traditional solubilizers such as Cremophore RH40 and Solutol HS15. It is an intriguing polymer to use as a carrier for the formulation of solid dispersions, theoretically speaking. Because it is non-ionic and hydrophilic, its solubility does not alter as the gastrointestinal system does. It is slightly surface active, a property which can be useful to maintain supersaturation of poorly soluble drugs in the gastrointestinal tract.Both organic and aqueous solutions can dissolve Soluplus®. Because of its solubility in volatile organic solvents, it can be used as a good candidate for spray drying and solvent evaporation to create dispersions. Together with another API, it creates stable solutions and is a good glass forming.

This study investigated the potential of Soluplus® to enhance the intestinal absorption of poorly soluble medications in addition to its solubilizing properties. Investigations into solid solutions of fenofibrate, itraconazole, and danazol showed that Soluplus® could improve drug flux across Caco-2 cell monolayers. The results aligned with the pharmacokinetic characteristics, including area under the curve (AUC) and maximum plasma concentration (Cmax). While no commercially available drug product containing solid solutions of poorly soluble drugs in Soluplus® exists, there has been increasing interest in developing Amorphous Solid Dispersions (ASDs) on a smaller scale. Initially designed as a carrier for solid solutions through processes like Hot Melt Extrusion (HME) or spray drying, Soluplus® has more recently been utilized in forming ASDs using methods such as high-energy ball milling or single-step 3D printing.For instance, Liu et al. employed the solvent evaporation method to prepare ASDs containing aprepitant and Soluplus®, achieving enhanced drug release rates Both organic and aqueous solutions can dissolve Soluplus®. Because of its solubility in volatile organic solvents, it can

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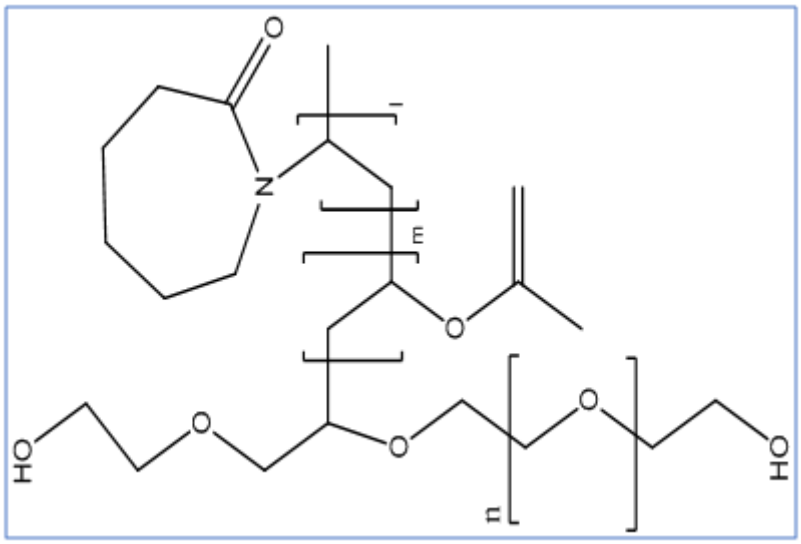

Fig no 1: - Structure of Soluplus

II. CHARCTERIZATION OF SOLUPLUS

The characterization of solupluswere given in Table no1

Table no.1: Characteristics of soluplus

Parameters	Characteristics
Appearance	White to yellowish free-flowing granules
Chemical Structure	Polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft co-polymer
Molecular Weight	Approximately 118,000 g/mol
Solubility	Soluble in various solvents including acetone, methanol, ethanol, dimethylformamide, and water
Critical Micelle Concentration	7.6 mg/L
Formulation Techniques	Can form amorphous solid dispersions using techniques such as hot melt extrusion and spray drying

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Applications	Suitable for capsule and tablet formulations
Solubility Enhancement	Enhances solubility of poorly soluble drugs
Processing Techniques	Amorphous solid solutions, hot melt extrusion, spray drying, drug-polymer layering
Bioavailability Enhancement	Demonstrated significant increase in bioavailability for poorly water-soluble APIs
Glass transition temperature (Tg)	~70 °C
Flow coefcient (Kv value; 1% ethanol)	31–41
Minimum ignition energy	10–30 mJ
Lower crystalline solution temperature (LCST)	~40 °C
HLB Approximately ~14	HLB Approximately ~14

III. APPLICATION OF SOLUPLUS AS CARRIER IN VARIOUS FORMULATION

A. Solid Dispersions

Ther Soluplus® is extensively used as a solubilizer and stabilizer in solid dispersionformulations. Its amphiphilic nature facilitates the creation of amorphous solid dispersions, improving the solubility of poorly water-soluble drugs. By enhancing dissolution rates and bioavailability, Soluplus® aids in overcoming formulation challenges associated with low drug solubility.A novel solubility enhancement excipient (Soluplus®) was investigated to improve the solubility and dissolution rate of Curcumin, a poorly water-soluble drug.

A.1 Stabillizer

Soluplus is highly effective in stabilizing pharmaceutical formulations due to its versatile properties and amphiphilic nature. Its capacity to form stable micelles and interact with both hydrophilic and hydrophobic components make it indispensable in stabilizing different dosage forms. In emulsions, Soluplus forms a protective layer around oil droplets, preventing them from merging and ensuring sustained stability. Moreover, in nanoparticle suspensions, Soluplus attaches to nanoparticle surfaces, preventing aggregation and sedimentation, thus maintaining particle uniformity. Within solid dispersion formulations, Soluplus forms a solid matrix around drug molecules, preventing their recrystallization and improving the stability of poorly water-soluble drugs. Additionally, it stabilizes supersaturated solutions by preventing drug precipitation, leading to prolonged supersaturation and enhanced drug absorption. Whether used in oral films or other formulations, Soluplus ensures structural integrity, preventing physical deterioration and ensuring consistent drug release over time. In summary, Soluplus serves as a versatile stabilizer critical for preserving the stability and effectiveness of pharmaceutical products across various formulations.

A.2 Solubillizer

Soluplus® has emerged as a versatile solubilizer within pharmaceutical formulations, drawing attention for its distinctive amphiphilic properties. Its ability to interact with both hydrophobic and hydrophilic elements make it an effective tool in enhancing the solubility of poorly water-soluble drugs. By integrating Soluplus® into formulations, it forms micelles or molecular dispersions, effectively dissolving drug molecules and thereby improving their bioavailability. This characteristic is particularly beneficial in addressing challenges associated with low aqueous solubility, paving the way for the development of innovative drug delivery systems like solid dispersions, nanoemulsions, and self-emulsifying drug delivery systems. Moreover, Soluplus® boasts compatibility with a wide array of active

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pharmaceutical ingredients and excipients, rendering it invaluable for formulators seeking to elevate the solubility and therapeutic effectiveness of poorly soluble drugs. For instance, recent research has explored the formulation of solid dispersions utilizing a novel graft copolymer, polyvinyl caprolactam–polyvinyl acetate–polyethylene glycol (Soluplus®), aiming to develop immediate-release formulations for a poorly water-soluble BCS class II drug. Carvedilol (CAR), a non-selective β-blocker with low water solubility, was selected as the model drug for investigation.

B. Tablets and Capsules:

As a binder and matrix-forming agent, Soluplus® plays a crucial role in preparation of oral solid dosage forms such as tablets and capsules. Its ability to form robust matrices helps in controlling drug release kinetics and ensuring formulation integrity. Moreover, Soluplus® contributes to the mechanical strength and disintegration properties of tablets, enabling precise dose administration and enhanced patient compliance.Soluplus plays a pivotal role as a direct compression aid in pharmaceutical tablet formulations, owing to its unique characteristics and versatile functionality. As a polymeric excipient, Soluplus facilitates the direct compression process by serving as a binder, disintegrant, and lubricant simultaneously. Its ability to form a cohesive matrix around drug particles promotes tablet integrity and uniformity, ensuring the consistent release of the active pharmaceutical ingredient (API). Furthermore, Soluplus aids in the rapid disintegration of tablets upon ingestion, enhancing drug dissolution and bioavailability. Its lubricating properties contribute to smoother tablet compression, reducing friction between the tablet blend and the compression tooling surfaces. Moreover, Soluplus offers formulation flexibility, as it is compatible with a wide range of APIs and excipients commonly used in direct compression formulations. Overall, Soluplus emerges as a valuable component in direct compression tablet manufacturing, streamlining the process while ensuring the quality, efficacy, and patient compliance of the final dosage form.[13]

B.1 Binder

Soluplus® serves as a highly effective binder in pharmaceutical formulations, particularly in the production of solid dosage forms like tablets and capsules. Its exceptional binding properties stem from its ability to form robust matrices when combined with other excipients and active pharmaceutical ingredients. As a binder, Soluplus® plays a crucial role in ensuring the integrity and mechanical strength of the final dosage form. It helps to hold the formulation together, preventing fragmentation or disintegration during manufacturing processes and subsequent handling by patients. Furthermore, Soluplus® contributes to the controlled release of drugs by regulating the dissolution kinetics of the dosage form. Its compatibility with a wide range of drug substances and excipients makes it a preferred choice for formulators seeking reliable binder options for various pharmaceutical formulations.Selecting the appropriate polymer for the extruded formulation is crucial, as it serves as both a carrier for the active pharmaceutical ingredient (API) and a binder that can deform readily while maintaining stability under processing conditions. In this form, the polymer acts as a meltable binder and release retardant. Therefore, the choice of polymer is pivotal in achieving the desired drug release profile during the design and optimization of melt extruded products.

B.2 Matrix forming agent

Soluplus® serves as an effective matrix-forming agent in pharmaceutical formulations, particularly in the development of solid dosage forms like tablets and capsules. Its ability to create strong and stable matrices is essential for controlling the release of active pharmaceutical ingredients (APIs) and ensuring the overall performance of the dosage form. When used as a matrix-forming agent, Soluplus® helps to bind together the various components of the formulation, including the API and other excipients, forming a cohesive structure that facilitates controlled drug release. Additionally, Soluplus® contributes to the mechanical strength and integrity of the dosage form, ensuring that it remains intact throughout manufacturing, storage, and administration to the patient. Overall, Soluplus® plays a critical role as a matrix-forming agent in pharmaceutical formulations, enabling the development of effective and reliable dosage forms with desired release profiles, In the present work a novel solubility enhancing excipient (Soluplus) was tested for its capability to improve intestinal drug absorption. BCS class II compounds danazol, fenofibrate and itraconazole were tested both in vivo in beagle dogs and in vitro in transport experiments across Caco-2 cell monolayers, the

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improvement of a solid dispersion compared to physical mixtures of the drugs and the excipient was correctly reflected by Caco-2 experiments.

B.3 Hot melt extrusion

Soluplus serves as a highly effective component in hot melt extrusion (HME) processes, offering numerous advantages in pharmaceutical formulation. As a thermoplastic polymer, Soluplus can be melted and processed at relatively low temperatures, making it well-suited for HME applications. During the extrusion process, Soluplus acts as both a binder and a carrier for active pharmaceutical ingredients (APIs), facilitating uniform distribution and controlled release. Its amphiphilic nature enables Soluplus to interact with both hydrophilic and hydrophobic components, ensuring compatibility with a wide range of drug substances. Furthermore, Soluplus enhances the stability of APIs, protecting them from degradation and oxidation during processing. By forming stable dispersions and solid solutions, Soluplus enables the formulation of various dosage forms, including tablets, films, and implants, with improved bioavailability and therapeutic efficacy. Overall, Soluplus emerges as a versatile and efficient material in HME processes, offering enhanced formulation flexibility, stability, and performance in pharmaceutical manufacturing, The aim of the study was to utilize the viscoelastic characteristics of polymer and drug-polymer blends in order to identify optimal processing parameters for creating amorphous solid dispersions through melt extrusion. In this research, the focus was on a poorly water-soluble medication, carbamazepine (CBZ), which was combined with Soluplus® as the carrier material [2] Itraconazole-soluplus solid dispersions with 50% (w/w) drug loading prepared by hotmelt extrusion (HME) were investigated.[17]

C. Nanoparticles and Microparticles:

Soluplus® finds application in the formulation of nano and microparticles for various drug delivery systems. Acting as a stabilizer and surfactant, it facilitates the dispersion and stabilization of drug particles, leading to improved colloidal stability and sustained release profiles. By optimizing particle size and surface properties, Soluplus® enables targeted drug delivery and enhanced therapeutic efficacy,To evaluate the characterized hydration method to prepare nanoparticles using Soluplus, a block copolymer with amphipathic properties, and distearoyl phosphatidyl ethanolamine (DSPE)-PEG2000.[13]

C.1Surfactant

Soluplus® exhibits surfactant properties that make it valuable in various pharmaceutical applications, particularly in formulations where emulsification or dispersion of hydrophobic compounds is required. As a surfactant, Soluplus® reduces interfacial tension between immiscible phases, such as oil and water, facilitating the formation and stabilization of emulsions or dispersions. This property is particularly beneficial in the formulation of lipid-based drug delivery systems, where Soluplus® aids in solubilizing poorly water-soluble drugs and enhancing their bioavailability. Additionally, Soluplus® can act as a stabilizer, preventing the coalescence or aggregation of droplets in emulsions and ensuring long-term stability of the formulation. Its versatility as both a surfactant and a polymer matrix-forming agent makes Soluplus® a valuable component in the development of advanced pharmaceutical formulations aimed at improving drug solubility, stability, and delivery.Soluplus, employed as a polymeric surfactant, significantly enhanced the dissolution and bioavailability of lopinavir in extrudate formulations compared to conventional solvent-evaporation methods. Its amphiphilic structure facilitated the formation of both hydrogen bonds and micelles with LPV, leading to improved drug permeability through biological barriers such as rat intestine and Caco-2 cell monolayers, primarily through P-glycoprotein (P-gp) inhibition.[12]

C.2 Solvent evaporation methods

soluplus-based solvent evaporation techniques offer advantages such as simplicity, scalability, and compatibility with a wide range of active pharmaceutical ingredients. This makes them particularly attractive for industrial production of nanoformulations. Additionally, Soluplus's amphiphilic nature facilitates the formation of stable colloidal dispersions, opening avenues for applications in areas like targeted drug delivery, sustained release formulations, and tissue engineering scaffolds. Overall, the utilization of Soluplus in solvent evaporation methods underscores its potential to revolutionize drug delivery and biomedical technologies, paving the way for innovative therapeutic solutions and improved patient outcomes.Two polymers were employed: the hydrophilic polymer PEG 4000 and the novel amphiphilic polymer Soluplus®. Utilizing the solvent evaporation method, SDs were

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prepared with Soluplus®, resulting in the formulation exhibiting the highest saturation solubility among those tested. solid dispersion of THF-PXM were prepared by solvent evaporation method.[17]

Ⅳ ADVANTAGES

1. **Enhanced Solubility**: Soluplus effectively boosts the solubility of poorly water-soluble drugs by forming micelles in water, which encapsulate hydrophobic drug molecules, thus improving their solubility and absorption.
2. **Improved Stability**: Soluplus enhances the stability of drugs, safeguarding them from degradation or aggregation by shielding them from environmental factors like light, heat, and oxidation.
3. **Streamlined Formulation Development**: Soluplus versatility and compatibility with various processing methods make it a valuable asset in developing different dosage forms such as tablets, capsules, and oral films.
4. **Advanced Drug Delivery**: Acting as a carrier in drug delivery systems like nanoparticles and microparticles, Soluplus's capacity to form stable dispersions makes it ideal for administering drugs through various routes.
5. **Taste-Masking**: Soluplus effectively masks the bitter taste of drugs in oral formulations, which is particularly beneficial for enhancing patient acceptance, notably in pediatric and geriatric populations.
6. **Convenient Handling**: Thanks to its favorable flow properties and compatibility with common pharmaceutical excipients, Soluplus is easy to handle during formulation processes.
7. **Regulatory Acceptance**: Having been incorporated into numerous pharmaceutical products and receiving regulatory approval in multiple countries, Soluplus's established track record eases its adoption in drug development and commercialization.

Ⅴ Disadvantage

1. **Moisture Absorption**: Soluplus has a tendency to absorb moisture from its surroundings, potentially compromising its stability and altering the characteristics of formulations over time. This poses concerns, particularly for the prolonged storage of pharmaceutical products.
2. **High Processing Temperatures**: Compared to certain other polymers, Soluplus necessitates relatively elevated processing temperatures. This could restrict its compatibility with drugs sensitive to temperature variations or specific processing techniques.
3. **Solubility Constraints**: Despite being generally soluble in various solvents, Soluplus may not exhibit optimal solubility for all applications. Certain drugs or excipients might have limited compatibility with Soluplus, thereby affecting formulation processes and final product performance.
4. **Potential Drug-Polymer Interactions**: There's a risk of interactions between drugs and Soluplus, akin to any excipient. Such interactions could influence the stability, bioavailability, or efficacy of the active pharmaceutical ingredient (API) in the formulation.
5. **Cost Implications**: While the pricing of Soluplus may fluctuate based on factors like volume and supplier, it could be relatively expensive compared to other polymers commonly employed in pharmaceutical formulations. This could potentially impact the overall cost-effectiveness of formulations.
6. **Regulatory Challenges**: Due to its status as a relatively novel polymer, there might be limited regulatory guidelines or precedents concerning the utilization of Soluplus in specific applications. This could present hurdles in obtaining regulatory approval for pharmaceutical products incorporating Soluplus.
7. **Processing Complexity**: The processing of formulations containing Soluplus may demand specialized equipment or techniques, especially for intricate dosage forms like nanoparticles or micelles. This additional complexity and associated costs could arise during the manufacturing process.

IV. CONCLUSION:

In conclusion, Soluplus, a polyvinyl caprolactam–polyvinyl acetate–polyethylene glycol graft copolymer, stands out as a promising pharmaceutical excipient offering a myriad of advantages for drug formulation and delivery. Its unique amphiphilic properties enable it to enhance solubility, stability, and bioavailability of poorly soluble drugs through various formulation approaches. From wet granulation to hot melt extrusion, Soluplus demonstrates versatility and compatibility with different processing techniques, making it suitable for a wide range of dosage forms including tablets, capsules, and oral films. The

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advantages of Soluplus are evident in its ability to improve drug solubility, enhance stability, streamline formulation development, and facilitate advanced drug delivery systems. Its taste-masking properties further contribute to patient compliance, particularly in populations sensitive to bitter taste sensations. Moreover, Soluplus has established regulatory acceptance, which eases its integration into pharmaceutical products. However, it's essential to acknowledge the challenges associated with Soluplus utilization, such as moisture absorption, high processing temperatures, solubility constraints, potential drug-polymer interactions, cost implications, regulatory challenges, and processing complexityunique characteristics are expected to yield further advancements in drug delivery systems, ultimately benefiting patients by improving therapeutic outcomes and treatment efficacy.

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