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A Comprehensive Review on Pharmaceutical Dosage Form

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Abstract: *Pharmaceutical liquid dosage forms are the liquid solutions that can be ingested, applied topically, or administered intravenously. These dosage forms are made up of a mixture of active medicines and excipients that produce a quick beginning of action after ingestion and provide the best therapeutic response in a given population. Pharmaceutical liquid dose forms are helpful and efficient for pediatric, elderly, and comatose patients who have difficulty swallowing solid dosage forms such as pills, capsules, and other medications. As a result, pharmaceutical liquid dosage forms are extremely important in the treatment and management of a wide range of disorders around the global. This article covers a wide range of topics related to pharmaceutical liquid dosage forms, including classification, benefits and drawbacks, excipients utilised in pharmaceutical liquid dosage forms, solubility enhancement techniques, and some of the instruments used to improve mixing.*

Keywords: Solubility; Bioavailability; Excipients; Lipophilicity.

I. INTRODUCTION

Pharmaceutical liquid dosage forms are those preparations that contains a combination of active drugs and excipients (emulsifying, dispersing, solubilizing, stabilising, suspending, wetting, thickening agent, preservative, sweetening agent, flavoring agent, and colouring agent) that are dissolved or suspended in appropriate solvents and used as a drug or medication [1]. It is the simplest type of pharmaceutical preparations for high absorption of medicinal drugs and rapid onset in which two components are enhanced to complete a liquid dosage form solute (a component that dissolves) and solvents (the medium in which the solute will dissolve). In pharmaceutical liquid preparations, parenteral routes are available in sterile forms, whereas oral liquids are non-sterile and can be administered via oral or parenteral routes (Injectable, inhalation, otic, tropical, nasal and ophthalmic). With the help of a chart, the classification of liquid dosage forms is presented below. Monophasic liquid dosage forms are the liquid solutions that comprise two or more components in a single phase. True solutions, which are homogeneous mixtures created by dissolving solute in long-term solvents, are also known as true solutions [2].

II. CLASSIFICATION OF LIQUID DOSAGE FORM

- Solution
- Syrup
- Mouthwash
- Linctus
- Gargles
- Lotion
- Throat paints
- Eye drops

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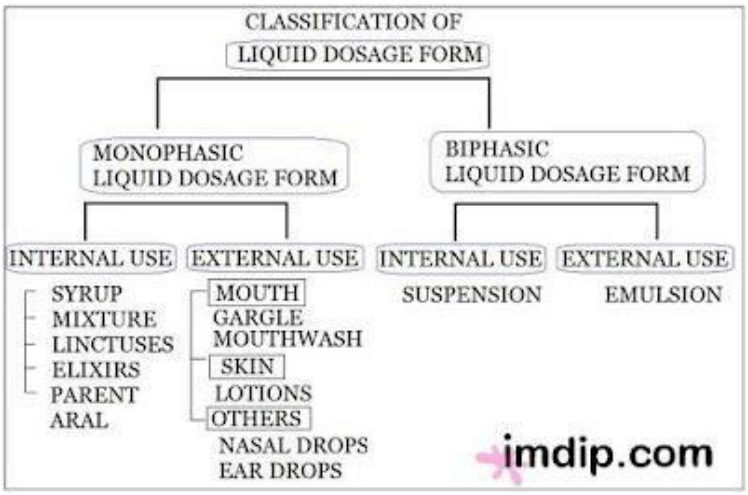

Fig 1. Classification Of Liquid Dosage Form.

2.1 Solutions

Solid materials(Fig.1) are dissolved in an appropriate solvent, which are homogeneous mixture containing one or more chemical compounds. Solutions are one of the oldest dosage forms and are made by dissolving a solid, liquid, or gas into a solvent in which the solute molecules are dissolved into a solvent such as water, alcohol or carbonated beverages [3].

A. SYRUP

Syrup(Table 1) is a sugar-in-water saturated aqueous solution with or without medicinal, ingredients. Syrups have a high percentage of sucrose (66.7% w/w I.P. and 85% w/v USP). Prepare sucrose 66.7% w/w syrup in filtered water, stirring constantly while heating. It's crucial not to let the temperature climb above 1600°C while heating [4]. After cooling, it's kept in a cool, dry area in a tightly sealed container to keep moisture and foreign particles out. Vitamins, sedatives, saline medicines, and antibiotics all use syrups in their compositions [5].

SIMPLE SYRUP L.P.	SIMPLE SYRUP U.S.P.
66.7% w/w solution of sucrose in purified water	85% w/v solution of sucrose in purified water.
It is prepared by hot process	It is prepared by cold process
It can be checked during the process by using saccharometer	It cannot be checked during the process.
Invert sugar. Sucrose heat → Invert sugar	Sucrose

Table 1 : Difference between simple syrup I.P and simple syrup U.S.P

B. MOUTHWASH

Mouthwashes are aqueous solutions with a pleasant taste and odour that are used to keep the buccal cavity clean and deodorised. Alcohol, glycerin, antimicrobial, colouring, and flavoring agents are all found in mouthwashes. Food particles caught deep inside the throat and mucous in the mouth can be eliminated with the help of mouthwashes with strong flavors and alcohol, which function by producing cough. Mouthwashes come in a variety of flavors, including antibacterial and anti-plaque mouthwashes, anti-cavity mouth rinses, and more. The antiseptic mouthwashes eliminate the bacterial plaque that causes bad breath, caries, and gingivitis, while the fluoride-containing mouthwashes protect against tooth decay [6]. It's primarily used for dental hygiene. In general, some firms suggest that when mouthwash is used, you should not drink water right away. However, mouthwashes are ineffective in removing plaque and bad breath, thus brushing and flossing are required [7]

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C. LINCTUS

Linctus is a viscous, monophasic liquid solution with a high syrup concentration that is used to treat cough and sore throat. It's made by dissolving citric acid in chloroform, adding peppermint water, amaranth solution, and syrup (as a carrier) to reach the desired volume [8]. However, the majority of linctus comprises chemicals that have expectorant, sedative, and antibacterial properties [9].

D. GARGLES

Gargles are aqueous concentrated solutions that are used to treat throat infections by coming into touch with the mucus membrane in the buccal cavity. Gargles are delivered in a concentrated form, but when used, they are diluted with warm water. Gargles are kept in an airtight jar with a plastic screw cover [10].

E. LOTIONS

Lotions are liquid preparations for application to the skin's surface. Lotions are applied to the skin's surface with cotton wool for purposes of protection, such as cooling and relaxing. Antiseptic, antibacterial, antifungal, moisturising, and protective substances are prescribed by dermatologists to treat or prevent skin problems [11].

F. THROAT PAINTS

Throat paints are the viscous liquid dosage form of medicaments which are used for the purpose of mouth and throat infections. Glycerin is typically used as a base in significant amounts to ensure that the medicine stays in contact with the mucous membrane for a long time and has a pleasant flavour.

G. EYE DROPS

Eye drops are ocular dosage forms of medications with drawbacks such as limited availability, frequent administration, pharmaceutical outflow through tears, unpredictability of dosages, and lacrimal fluid. The inherent physiology of the eye continues to make ocular drug distribution difficult [12]. The efficient removal mechanism at the site of action (rapid tear turnover, blinking) and low corneal permeability combine to diminish the efficacy of ophthalmic formulations and restrict drug bioavailability to less than 5%.

H. BIPHASIC LIQUID DOSAGE FORMS

Biphasic liquid dosage forms are ones that have two phases in them. This comprises the medicine that has been dissolved as well as the solvent (vehicle). There are two types of biphasic liquid dosage forms.

- Suspension
- Emulsion

III. SUSPENSION

Suspensions are biphasic liquid dosage forms of medication in which the internal phase is uniformly distributed with finely divided solid particles in a liquid dispersion medium over a period of 0.5 to 5 minutes. In pharmaceutical solutions, solid particles act as a disperse phase, while liquid vehicles act as a continuous phase. The external phase, also known as the suspending medium. Pharmaceutical suspension formulations are done for the following reasons.

- To improve the drug stability of the suspensions.
- To reduce the bitterness.
- The medication is insoluble in the delivery medium in this formulation.
- To achieve long term medication release (sustained release).

Classification of Suspension: Suspensions are categorised using the following framework:
Determined by administration route

- Oral
- Parenteral
- Topical

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Oral Suspensions

For oral administration, an oral suspension consists of undissolved particles and active substances suspended in sweetening, flavoring, or viscous vehicles with therapeutic agents. Oral suspensions are commonly used to treat oral fungal infections. "Oral suspensions allow for dose flexibility and are cost-effective when a patient requires dose titration, however many pharmaceutical medications are not available as oral suspensions [13]. Insoluble components are suspended in a dispersion media with suspending agents to create oral suspensions. Suspending agents are used to help disperse powders evenly throughout the preparation and avoid particle flocculation [14].

Parenteral Suspensions

Parenteral suspension are sterile preparations that are intended to be administered directly into the systemic circulation of people. Parenteral suspensions are insoluble medication particles dispersed in a heterogeneous system that must be resuspended in an aqueous or vegetable oil vehicle before being administered to patients.

Topical Suspension

Tropical suspensions are liquid treatments that contain solid particles suspended in a liquid carrier for skin application.

Emulsion

Types of Emulsion

The two basic types of emulsions such as

- O/W (oil dispersed in water)
- W/O (water dispersed in oil).

Oil-In-Water Emulsions (O/W)

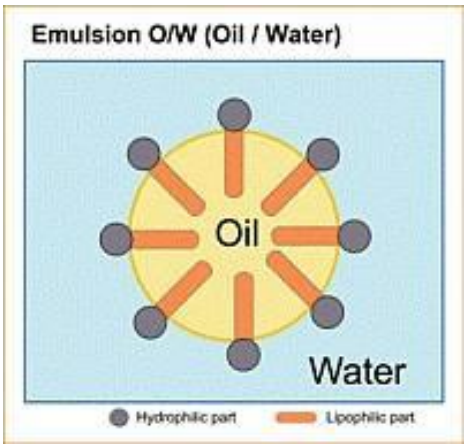

Figure 2: Oil in water types of emulsion.

Pharmaceutical emulsions are made up of a mixture of oil drop lets scattered throughout the aqueous phase. Fats and oils for oral administration are always manufactured as oil-in-water (O/W) emulsions shows in figure 2, whether as carriers for oil-soluble medications or as medicines in their own right. They're non-greasy and easy to wipe away from the skin's surface [15]. They are applied physically to provide a cooling effect and internally to mask the oil's unpleasant taste.

Water-In-Oil Emulsions (W/O)

W/O emulsions (water-in-oil emulsions) are medicinal emulsions in which water is scattered as globules in oil continuous phase shows in figure 3. Water-in-oil emulsions have an occlusive action, which hydrates the stratum corneum and prevents the evaporation of eccrine secretions. They're oily but not watersoluble, and they're used to maintain moisture from evaporating from the skin's surface while cleansing it of oil-soluble dirt [16]. Example: Cold cream.

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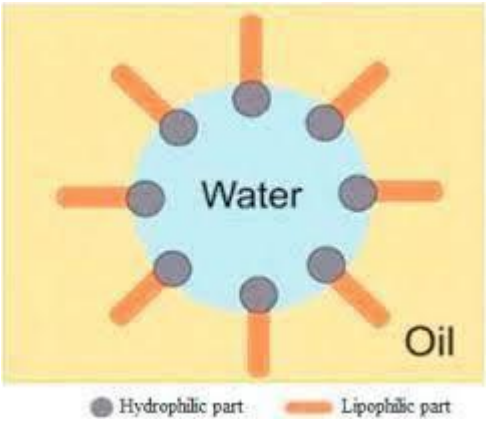

Figure 3: Water in oil types of emulsion

IV. SELECTION, QUALITIES AND FUNCTIONS OF EXCIPIENTS

Excipients are substances in a formulation that are not active compounds. They can be natural or synthetic substances added with the drug for long-term stability, formulations including the drug, or therapeutic augmentation of the drug in the final dosage form. Excipients are non-active or inactive chemicals that are added to pharmaceutical compositions during the manufacture of dosage forms. They have no therapeutic effect but are required to alter the drug's and dosage form's function. Because they are inert in nature, they have no pharmacological impact. It mostly aids in the manufacturing process by preventing nonstick qualities and maintaining in vitro stability, such as aiding flow-ability or aggregating over time. As a result, excipients are an essential component of pharmaceutical dosage forms, and they are included in higher proportion in most formulations than the medication.

Although excipients are considered inert substances, several of them have been discovered to have a direct impact on dissolution rate and medication absorption. Some excipients were discovered to have some efficacy in terms of promoting penetration into tumor cells. Specific investigations validated concerns about the prevalence of some negative effects connected with the presence of certain types of excipients, such as sugar and lactose; paraben and menthol are linked to hyperglycemia, stomach cramps, hypersensitivity reactions, and laryngeal spasms in newborns, respectively.

4.1 Selection of Excipients

It depends on upon its physicochemical properties, characteristics of active drug and route of drug administration. Regulatory acceptance, material consistency, source, cost and availability, stability and compatibility issues, pharmacokinetic parameters, permeation characteristics, segmental absorption, behavior, drug delivery platform, intellectual property issues, and so on are all factors to consider. Knowledge of API, excipients, their interactions, and process parameters is essential for a successful pharmaceutical formulation. or to improve the chemical stability of a drug. A co-solvent boosts a drug's solubility. The dielectric constant of an ideal co-solvent should be between 25 and 80. A water/ethanol blend is the most generally utilised solution that will handle this range. When administered for oral or parental use, it should not cause toxicity or irritancy. Sorbitol, glycerol, propylene glycol, and syrup are some of the other co-solvents.

A. Solubilizers

Solubilizers are a type of fungicide that to improve the drug's solubility, make the following pH adjustments: By incorporating a buffer into the formula. To control potential pH variations, buffers act by binding hydrogen formulations. In acids, buffers bind hydrogen ions, while in bases, they donate hydrogen ions. The acid-base form's suitability for use in oral liquids, the stability of the medicine and excipients in the buffer, and the buffer's compatibility with the container should all be considered when choosing a suitable buffer. The possible reactivity between excipients and medication is determined by the stabilising impact of buffers. Carbonate, citrate, tartarate, and phosphate salts, for example, may precipitate with calcium ions to generate sparingly soluble salts. Temperature, ionic, strength, dilution, and the number and kind of co-valents present are all factors that can change the pH of a solution. The pH of acetate

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buffers, for example, is known to rise with temperature, but the pH of boric acid buffers is known to fall with temperature. It's crucial to understand that the medicine in solution might act as a buffer. If the drug is a weak electrolyte like salicylic acid or ephedrine, adding a base or acid will produce a situation where the drug can operate as a buffer. Example: phosphate buffers, acetate buffers, citric acid phosphate buffers etc. Co-solvency is achieved by mixing a water miscible solvent with a medication that has a high solubility. Co-solvent is a type of solvent. When a Complexing agent is added to a solution, it forms a complexation with the drug.

B. Preservatives

A major issue with aqueous-based liquid dosage forms is microbial contamination. In such instances, the use of preservatives becomes unavoidable to inhibit the growth of microorganisms during production and storage. In fact, developing a preservative-free formulation is desirable to avoid the negative effects of these excipients. Most of the preservatives are bacteriostatic rather than bactericidal and come in both acid and non-acid forms [17]. The following conditions must be met by preservatives: Efficacious against a wide range of bacteria. For the duration of the product's life, it must be physically, chemically, and microbiologically stable.

4.2 Types of Preservatives

- Acidic: Phenol, benzoic acid, sorbic acid
- Neutral preservatives: Chlorobutanol, benzyl alcohol
- Quarternary ammonium compounds : Benzalkonium chloride.

Stabilizers

- Suspending agents

Physical stability

- Sweeting agent

Solubility enhancement techniques Surfactants

The traditional strategy to solubilizing a poorly soluble chemical is to lower the interfacial tension between the surface of the solute and the surface of the solvent to improve wetting and salvation contact. Surfactants such as Polyglycolyzed glycerides, Tweens, Spans, Polyoxyethylene stearates, and synthetic block copolymers such as Poly (propylene oxide)-poly (ethylene oxide)-poly (propylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene. The use of amphiphilic surfactants improves drug solubility by lowering surface tension between the drug and the solvent, improving wetting qualities, and micellar solubilization [18].

Salt Formation

For decades, salt production of poorly soluble medication candidates (weak acids and bases) has been used to improve solubility. It works effectively in both parenteral and other liquid formulations as well as solid dose forms. Between 1995 and 2006, the FDA approved over 300 novel chemical entities for marketing, 120 of which were salt forms. Furthermore, hydrochloric acid was used to produce 54 of the 101 approved salts of basic medicines, indicating that hydrochloride was the most common salt type. An acidic or basic drug's water solubility as a function of pH determines whether the chemical will form appropriate salts [19]. The pH-solubility interrelationships also determine what counter ions are required to create salts, how quickly the salts dissociate into their free acid or basic forms, how salts dissolve under varied GI pH conditions, and if common ion influences salt solubility and dissolution rate.

Co-solvents

A co-solvent system is a concoction of miscible solvents that is commonly employed to dissolve lipophilic medicines. Polyethylene glycol 400 (PEG 400), ethanol, propylene glycol, and glycerin are currently the water-soluble organic solvents. For example, Pfizer's Procardia (nifidipine) soft gelatin capsules contain glycerin, peppermint oil, PEG 400,

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and sodium saccharin. Long-chain triglycerides (peanut oil, corn oil, soybean oil, sesame oil, olive oil, peppermint oil, hydrogenated vegetable oil, and hydrogenated soybean oil), medium-chain triglycerides (Miglyol 812), beeswax, d—tocopherol (vitamin E), and oleic acid are among the water insoluble solvents. Progesterone, a water-insoluble steroid that is soluble in peanut oil, is a commercially accessible example of this method [20].

V. CONCLUSION

In today's era, the world population is suffering from several diseases as the result the number of increasing patients having difficulties in swallowing tablets and capsules. In that case liquid dosage forms works effectively in both older and paediatric patients. There is creates a problem for the healthcare professionals, especially for the pharmacists who is often required to provide a monophasic and biphasic liquid preparations.

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