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Review Article

Study of Natural Excipients in Liquid Dosage Forms

A. Krishna Sailaja, Bayya Hrushitha, Bandra Ausha, Chinthakunta Deepika Reddy, Kommireddy Tejaswini

Department of Pharmaceutics, RBVRR Women's college of Pharmacy, Hyderabad.

***Corresponding Author:** A. Krishna Sailaja, Bayya Hrushitha, Department of Pharmaceutics, RBVRR Women's college of Pharmacy, Hyderabad.

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Abstract

Liquid dosage forms can be administered by oral and parenteral (injectable, inhalation, ophthalmic, optical, nasal, and topical) routes. Oral liquids are nonsterile, whereas liquids administered by the parenteral route are both sterile and nonsterile mixtures. The liquid formulations may be provided as reconstitute powders or as ready-to-use liquids. This article describes manufacturing procedures, quality assurance and control, physicochemical parameters that affect liquid formulation characteristics, and regulatory requirements for the production of both sterile and nonsterile liquids.

Kew Words: sportswomen/female athletes; single combats; freestyle wrestling; classical wrestling; sexual somatotypes; masculinization

Introduction

Liquids are pourable dosage forms and can be solutions or dispersions. In contrast to liquid dispersions, which can be two-phase or multi-phase systems made up of one phase dispersed through another phase or phases, pharmaceutical solutions are transparent, uniform, single-phase systems that contain one or more drug ingredients dissolved in one or more solvents. Micelles (surfactant solutions), lipid vesicles (liposomes), solid particles (suspensions), and oil droplets (emulsions) can all make up the dispersed phase.

Figure 1: Liquid dosage forms

Advantages of liquid dosage forms

- For individuals who have trouble swallowing pills or capsules, such as elderly or paediatric patients, liquid dose forms (for oral administration) are the best option.
- They have positive psychological impacts and are aesthetically pleasing.
- . Sweetened, coloured, and flavoured vehicles can be used to provide medications with an unpleasant and bitter taste.
- Compared to solid dosage forms like tablets and capsules, there is more dosing flexibility. Measuring a varied volume makes it simple and convenient to change the medication substance's dosage.
- Compared to tablets and capsules, liquid dosage forms are more quickly absorbed when taken orally.

- Hygroscopic and deliquescent medicaments which are not suitably dispensed in solid dosage forms can easily be given in liquid dosage form.
- The products like adsorbents and antacids are more effective in liquid dosage form.
- The liquid dosage form is expected for certain types of products like cough medicaments [1]

Formulation	Description
Syrups	Syrups are concentrated, aqueous preparations of sugar or sugar substitutes intended for oral administration of bitter-tasting drug substances
Oral solutions	Oral solutions are liquid preparations intended for oral administration. Oral solutions contain one or more active substances and inactive excipients
Elixirs	Elixirs are clear, sweetened, hydroalcoholic (5% 40%) solutions intended for oral use. Nonmedicated elixirs are employed as vehicles for medicated elixirs.
Ophthalmic solutions	Ophthalmic liquid products are sterile preparations intended for application to the conjunctiva, conjunctival sac, or eyelids.
Nasal solutions	Most nasal solutions are administered as nasal drops or sprays for local and systemic purposes.
Enemas	Enemas are oily or aqueous solutions that are administered rectally.
Suspensions	Suspension is a liquid dosage form of poorly water-soluble drug(s) dispersed in a liquid medium
Emulsions	Emulsions are liquid disperse systems consisting of two immiscible phases, one of which is dispersed as globules in the other liquid phase.[37]

Table: -1 Different types of dosage forms

SYRUPS: Syrups are concentrated, aqueous preparations of p0370 sugar or sugar substitutes intended for oral administration of bitter-tasting drug substances. Nonmedicated or flavoured vehicles (syrups) are syrups that contain flavouring compounds without the use of drugs. When making medicated syrups or impromptu compounding prescriptions, these syrups act as tasty carriers for medicinal ingredients that will be added later. The taste of pharmacological compounds is covered up by syrup carriers with the right amount of sweetness and viscosity.

Advantages of natural syrups:

- No side effects
- Harmless
- Easily available
- Easy to adjust the dose for child's weight
- No nursing is required, which main and the patient can take it with no help
- The liquid dosage form is executed for products like cough medicines.
- Herbs Grow in common place
- Antioxidant by retarding the oxidation as sugar is Hydrolysed in to cellulose and dextrose
- Good patient compliance especially paediatrics as syrup is sweet in test
- It is a preservative by retarding the growth of bacteria, fungi and mould as osmotic pressure [2]

Flavours	Orange oil, Raspberry, Neroli oil, Peppermint oil
Antioxidant	Peppermint, Rosemary, Cinnamon, Saffron
Sweeteners	Honey, Sucrose, Glycyrrhizin, Hesperidin
Preservatives	Clove oil, Tea tree oil, Ginger oil
Colourants	Carminic acid, Tyrian purple, Alizarin, Indigo [39]

Table 2: - Excipients Used in Syrups:

Flavours: Flavors are those agents which are used for masking the taste and also hide the unpleasant taste or Oduor of a dosage form. Flavors enhance the likelihood of medicines and make them more compatible for administration to a patient. Use of flavors in dosage forms make children take medicines without any problem. Flavoring agents used in different dosage forms are tablets, pills, pellets, capsules, pastes, syrups, emulsions, suspensions, mouth washes etc. Natural flavoring agents give the realistic flavor with good oduor and have no negative effect on human as well as environment.

Ideal properties of natural flavoring agents:

- Staying power
- Sillage
- Packaging
- Vitality/ Freshness [3]

Excipient	BS	Family	Synonym	Use	Formulation
Orange oil	It comes from the rind of sweet orange fruit Citrus sinensis	Rutaceae	Citrus aurantium	Flavor	Emulsions
Raspberry	It is obtained from the fruits of Rubusrosi folius	Rosaceae	Cane fruit	Flavor	Syrups Suspensions Serums
Neroli oil	It is extracted from flowers of citrus aurantium var	Rutaceae	Citrus bigaradia oil	Perfume	Oils
Peppermint oil	It is obtained from the flowering parts and leaves of the peppermint plant	Lamiaceae	Menta pepperita	Perfume	Oil roll on [41]

Table 3: - Details of various natural flavoring agents as excipients in liquid dosage forms

Sweetening Agent: Sweetening agents are chemical substances that are added to either mask the unpleasant taste or enhance the perception of a sweet taste in some oral pharmaceutical preparations such as tablets, syrup, suspension etc. Also, Sweetening agents are called sweeteners. Importantly, sweetening agents are the common excipients for paediatrics

Ideal properties of natural sweetening agent:

- It must be reasonably sweet, at least as sweet as sugar, with no lingering after
- It must be economical to produce and be cheaper than sugar for the consumer
- It should be preferably non-caloric and have no nutritive value.
- It must be non-toxic with no dangerous side effects such as carcinogenicity or teratogenicity. It should not have any synergistic detrimental effects with drugs or in the presence of foods or beverages.
- The metabolite must also be non-toxic with.
- It must be thermostable and not decompose during cooking or in the presence of sunlight.
- It must be soluble in water.[4]

Excipient	BS	Family	Synonym	Use	Formulation
Honey	It is a secretion deposited from the honey comb by the Apis mellifera	Apidae.	Madhu	Sweetening agent	Syrups
Sucrose	It is a ddisaccharide sugar obtained mainly from the cane juice of saccharum officinarum	Graminae	Beet sugar, cane sugar	Sweetening agent	Syrups, lozenges, Injections
Glycyrrhizin	It is a penta-cyclic triterpenoid saponins glycoside obtained from root, stolon of Glycyrrhiza glabra	Leguminosae	Liquorice	Sweetening agent	Cough mixtures

Table 3: - Details of various natural sweetening agents as excipients in liquid dosage forms

Colorants: Colorants or coloring agents are commonly used for imparting distinctive appearance to the pharmaceutical dosage form. Colorants are agents used in the pharmaceutical preparations like cosmetics to give aesthetic appearance to the dosage forms. Dosage forms that are colored are tablets (either the core itself or the external coating) hard or soft gelatin capsules (the capsule shell or coated beads) oral liquids, toothpastes, topical creams, ointments and salves.

Ideal properties of natural coloring agent:

- Non-toxic and have no physiological activity
- Free from harmful impurities
- High coloring property should be there.
- Unaffected by light, tropical temperature, hydrolysis
- Compatible with medicaments and does not interfere with them
- It occurs as red crystals in pure state when recrystallized from light petroleum.[5]

Excipient	BS	Color	Synonym	Use	Formulation
Carminic acid	It is obtained from insect Coccus cacti	Bright red	Carmin	Coloring agent	Emulsions
Tyrian purple	It occurs by air oxidation of Murex brandaris(snail)	Bluish purple	Royal purple	Coloring agent	Emulsions Oils
Alizarin	It comes from the roots of madder plant, Rubia tinctorum	Red	Mordent red 11 Turkey red	Coloring agent	Emulsions
Indigo	It comes from the leaves of Indigofera tinctoria plant	Dark blue		Coloring agent	Tinctures [44]

Table 4: - Details of various natural coloring agents as excipients in liquid dosage forms

Preservatives: Preservatives are usually used to minimize the shelf life of several food products and pharmaceuticals. Preservatives are vital to avoid the alteration and degradation of microorganisms during storage. Particularly in those with greater water content [6]

Ideal properties of natural Preservatives:

- It should not be irritant.
- To maintain product consistency.
- To maintain palatability and wholesomeness.
- It should not be toxic.
- It should be stable (physically and chemically).
- It should be compatible with all other ingredients
- It should be act as good antimicrobial agent
- It should be potent in action.
- It should have higher shelf life

Excipient	BS	Family	Synonym	Use	Formulation
Clove oil	Buds of myrtaceous syzygium	Myrataceae	Eugenol	Preservative	Mouthwashes Oils
Tea tree oil	Derived from the leaves of the melaleuce alternifolia plant	Myrtaceae	Melaleuca	Preservative	Essential oils
Ginger oil	It consists of dried rhizomes of Zingiber officinale	Zingiberacae	Zingiber	Preservative	Syrups[8]

Table 5: - Details of various natural flavoring agents as excipients in liquid dosage forms

Suspensions: A liquid dosage form of a medicine or drugs that are poorly soluble in water and distributed in a liquid medium is called a suspension. Particles in an ideal suspension are evenly distributed and do not aggregate. Particles should be gently stirred to resuspend them even if sedimentation takes place. Aqueous suspensions are intended for oral, ophthalmic, inhalation, and topical applications, while oil-based suspensions have parenteral applications (e.g., sustained-release depot formulations). Oral and topical suspensions contain a high concentration of solids in the range of 5%50% solid particles, while parenteral suspensions incorporate 0.5%25% solid particles. Based on particle size, suspensions are classified as coarse or colloidal dispersions, with the former containing particles of mean diameter in the range of 125 μM, and the latter containing particles with a mean diameter less than 1 μM [7]

Flocculated suspension: n flocculated suspensions, the particles organise into loose aggregates that resemble networks. These suspensions exhibit a rapid rate of sedimentation, yet no hard cake forms because the particles are loosely packed. Re-dispersing such flocs is not difficult.

Deflocculated suspension: Defl**o**cculated suspension: Suspensions consist of uniformly scattered particles in the aqueous phase. In deflocculated suspensions particles exist as separate entities and exhibit a slow rate of sedimentation. Sediments tend to form a hard cake which is difficult to re-disperse.

Advantages of natural suspensions:

1. Drug compounds that are insoluble in water can be made into suspensions.

2.they prolong drug release rates;

3. they reduce the rate at which hydrolytic drug molecules degrade; · medications with extremely poor solubility are effectively prepared as suspensions.

4. suspension for patients with swallowing difficulties can be formulated as palatable suspensions. Some of the disadvantages include (a) aggregation of particles; (b) complex manufacturing processes.[8]

Wetting agent	Lecithin, Sorbitan monolaurate, Sorbitan monooleate, Ceto stearyl alcohol
Suspending agent	Kaolin, Sesame oil, Hectorite, Ceratonia
Preservatives	Clove oil, Neem oil, Ginger oil, Tea tree oil
Antioxidant	Peppermint, Rosemerry, Cinnamon, Saffron [9]

Table 6: - Excipients used in suspensions:

Suspending Agent: A suspension is a colloidal dispersion in which a solid is dispersed in a continuous liquid phase. The continuous phase is frequently referred to as the exterior phase, and the scattered solid phase as the interior (disperse) phase. In a suspension, the solute particles are fairly large in size.

Ideal properties of natural suspending agent:

- A suspension is a heterogeneous mixture.
- The size of solute particles in a suspension is quite large.
- It is easy to see the particles in a suspension
- A filter paper does not allow particles in a suspension to flow through it. Filtration can therefore be used to separate a suspension.
- There is instability in the suspension. After a while, the particles in a suspension settle.
- A suspension scatters a beam of light passing through it because of its large particle size [10]

Excipient	BS	Family	Synonym	Use	Formulation
Kaolin	Kaolin is a hydrated aluminum silicate obtained by mining naturally occurring mineral deposits	-	Argilla bolus alba China clay	suspending agent	mixtures
Sesame oil	Sesame oil is obtained from the ripe seeds of the sesamum indicum plant	Pedaliaceae	Benne oil, gingelly oil	suspending agent	solutions, emulsions, suspensions
Hectorite	Natural deposits it is further processed to remove grit and impurities	-	Astratone40 Bentone CT	suspending agent	Creams lotions
Ceratonia	It is obtained from the ground endosperms from the seeds of the locust bean tree Ceratonia siliqua and belonging to the family Leguminosae	Leguminosae	Algaroba,	suspending agent	Emulsions [41]

Table 7: - Details of various natural suspending agents as excipients in liquid dosage forms

Antioxidant: Antioxidants are compounds that inhibit oxidation (usually occurring as autoxidation), a chemical reaction that can produce free radicals. Antioxidants are frequently added to industrial products, such as polymers, fuels, and lubricants, to extend their usable lifetime.

Ideal properties of natural anti-oxidants:

1.It should be stable

2.It should be effective in low concentration

3. It should be compatible

4.It should be non-toxic [11]

Excipient	BS	Family	Synonym	Use	Formulation
Rosemary oil	Rosemary is obtained from the flowering tops of leafy twigs of Rosmarinus officinalis	Lamiaceae	Rosmarinus officinalis	antioxidant	Oils

Cinnamon	The Cinnamon consist of dried bark, freed from the outer cork and from the underlying parenchyma	Laureceae	Ceylon cinnamon, cinnamon bark	antioxidant	Gargles
Thyme oil	It is extracted from the flowering parts of the mint plant	Lamiaceae	Thymus vulgaris	antioxidant.	Mouth washes

Table 8: - details of various natural antioxidants as excipients in liquid dosage forms

Emulsions: Emulsions are liquid disperse systems consisting of two immiscible phases, one of which is dispersed as globules in the other liquid phase [50]. The presence of an emulsifier stabilises the two phases of emulsions. While particle diameters as tiny as 0.01 µM and as large as 100 µM are possible, the dispersed phase's droplet diameter ranges from roughly 0.1 to 10 µM. are not uncommon. The consistency of emulsions ranges from that of a liquid (e.g., fat emulsions) to a semisolid (e.g., ointments and creams]

Advantages of emulsions:

- To solubilise hydrophobic or oil soluble drugs
- To enhance drug absorption through
- To improve medication absorption through topical application
- To cover up the unpleasant taste and smell of medications.
- To enhance palatability of nutrient oils [12]

Antioxidant	Peppermint oil, Rosemary oil, Cinnamon oil,Thyme oil
Emulsifying agent	Cottonseed oil, Faba bean oil, Mustard oil, Palm oil
Preservatives	Clove oil,Neem oil, Cumin seeds, Cayenna pepper, Ginger oil, Tea tree oil [13]

Table 9: -Excipients Used in Natural Emulsions:

Emulsifying Agent: Emulsions are liquid disperse systems consisting of two immiscible phases, one of which is dispersed as globules in the other liquid phase. While particle diameters as tiny as 0.01 µM and as high as 100 µM are not unusual, the dispersed phase's droplet diameter ranges from roughly 0.1 to 10 µM. While particle diameters as tiny as 0.01 µM and as high as 100 µM are not unusual, the dispersed phase's droplet diameter ranges from roughly 0.1 to 10 µM to a semisolid (e.g., ointments and creams]

Ideal properties of emulsifying agent:

- All the characteristics of a colloidal solution, such as electrophoresis, the Tyndall effect, and Brownian movement, are present in emulsions.
- The globules coagulate when electrolytes containing polyvalent metal ions are added, indicating their negative charge.
- The globules coagulate when electrolytes containing polyvalent metal ions are added, indicating their negative charge.
- . It has a range of 1000 to 10,000 Ă. In contrast, the size is smaller than that of particles in suspensions.
- In contrast, the size is smaller than that of particles in suspensions. Demulsification is the term for this procedure.[14]

Excipient	BS	Family	Synonym	Use	Formulation
Cotton seed oil	It is obtained from the seed of cultivated varieties of Gossypium hirsutum linn	Malvaceae	Refined cotton seed oil	Emulsifying agent	oils
Faba bean protein	It comes from the Faba bean	Leguminoseae	Broad bean	Emulsifying agent	Gels
Mustard oil	It is obtained from the seeds of mustard plant	Brassicaceae	-	Emulsifying agent	Essential oils Creams
Palm oil	the oil obtained from the pulp of the fruit of the oil palm Elaeis guineensis jacq	Aceraceae	Cage soft Dynasan 60	Emulsifying agent	Emulsions [15]

Table 10: - Details Of Vari ous Natural Emulsifying Agents as Excipients In Liquid Dosage Forms

Conclusion:

Pharmaceutical excipients derived from natural sources have attracted a great attention in developing convectional dosage forms and novel drug delivery systems. The use of natural excipients is steadily increasing day by day due to the side effects of synthetic excipients. Hence natural excipients are being preffered over synthetic as they are cheap, biodegradable and enhance the bioavailability, stability, safety, efficacy and patient compliance. Therefore, there is going to be a great interest in natural excipients to obtain a better dosage form.

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