IJRAR.ORG E-ISSN: 2348-1269, P-ISSN: 2349-5138

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYTICAL REVIEWS (IJRAR) | IJRAR.ORG

An International Open Access, Peer-reviewed, Refereed Journal

A COMPREHENSIVE REVIEW ON LIQUID DOSAGE FORM

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Abstract: Liquid oral dosage forms are a versatile and commonly used method of medication administration, particularly for patients who struggle with swallowing tablets or capsules. They provide distinct advantages such as ease of swallowing, accurate dosing, and rapid absorption. This review explores the different types of liquid oral dosage forms, their advantages and limitations, and recent technological innovations that have advanced their effectiveness and patient acceptance. Despite their benefits, challenges such as stability concerns, dosing errors, and taste issues remain significant hurdles. Nonetheless, the continuous development in formulation technologies has the potential to address these challenges and further improve patient adherence and therapeutic outcomes.

IndexTerms – Liquid dosage form, Monophasic, Biphasic, Suspension, Emulsion.

INTRODUCTION

Liquid dosage forms are pharmaceutical preparations where an active drug is combined with non-active components such as solvents and additives to create a liquid 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). [2]

They are administered by oral and parenteral (injectable, inhalation, ophthalmic, optic, nasal and topical) routes. Oral liquids are non-sterile, whereas liquids administered by the parenteral route are available as sterile and non-sterile formulations. In the preparation of liquid dosage form, a lot of additive ingredients are used such as vehicles, stabilizers, preservatives, suspending agents, emulsifying agents, solubilizers, colours, flavours, etc.[3]

Liquid oral dosage forms offer advantages such as dose flexibility and ease of swallowing for children, they may indeed require ingredients that are not child-friendly. Some compounds or excipients commonly used in liquid formulations, such as alcohol, artificial sweeteners, or certain preservatives, may not be suitable for young children due to safety concerns or potential adverse effects.[4]

ADVANTAGES OF LIQUID DOSAGE FORMS

1. Dose can be adjusted by measuring a specific volume.
2. Patients having difficulty in swallowing tablets and capsules, can easily swallow solution or syrups eg., cough syrup.
3. Taste of unpleasant drugs can easily be masked by sweeteners and flavouring agents.
4. Drugs such as potassium chloride can produce peptic ulcers when administered in the tablet form but prevent this side effect, when administered in liquid form.
5. The therapeutic response is faster than solid dosage form.[5]

DISADVANTAGES OF LIQUID DOSAGE FORMS

1. The shelf life is less in liquid dosage forms.
2. Liquid is comparatively difficult during handling and storage.
3. Solutions are quickly degraded by microorganisms therefore; preservatives are intended to be added into the formulations
4. Inconvenient for travelling purposes as there is a problem of spillage.
5. Ingredients are usually more susceptible to degradation.[6]

CLASSIFICATION OF LIQUID DOSAGE FORM

Liquid dosage form is often classified into two major groups i.e, monophasic and biphasic liquid dosage form.

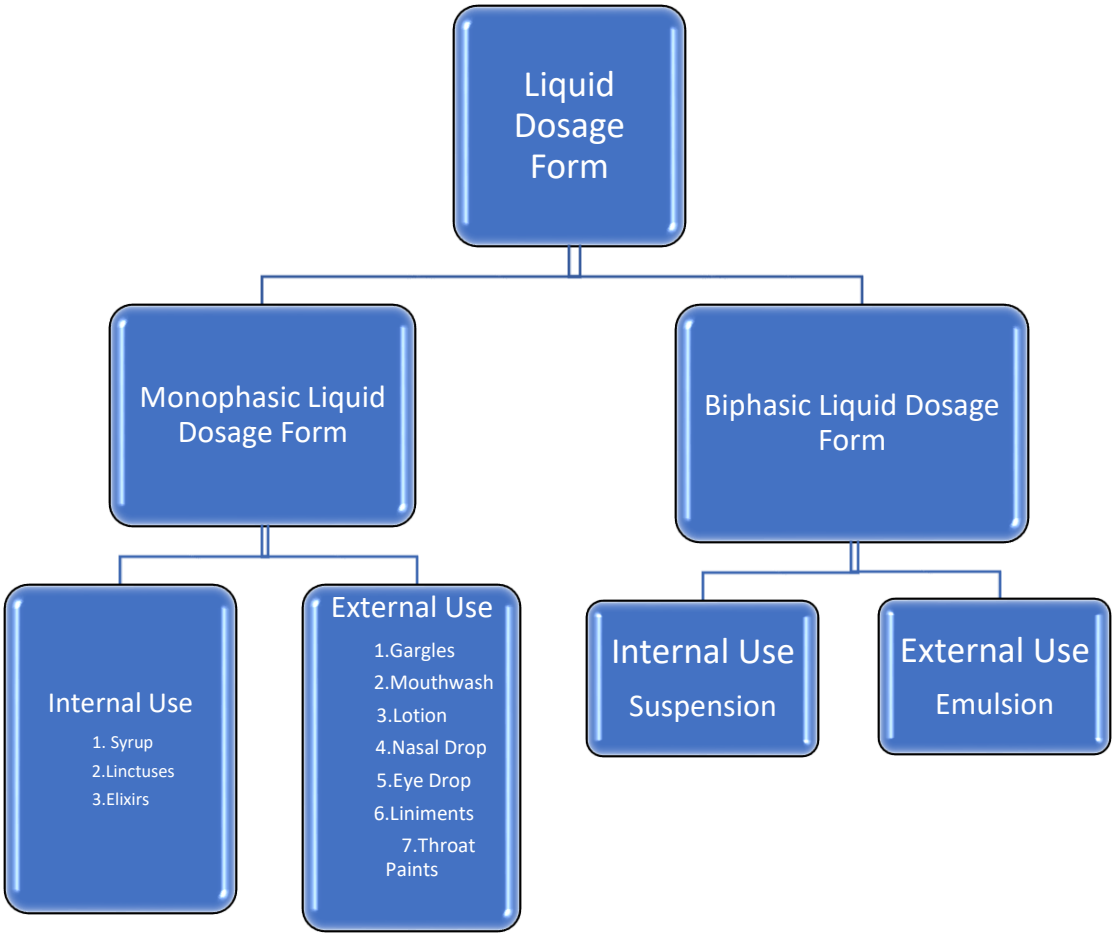

fig 1: classification of liquid dosage form

MONOPHASIC LIQUID DOSAGE FORM

A liquid preparation with two or more compounds in a single-phase system represented by the real solution is referred to as a single-phase equilibrium form. Actual solutions are made by dissolving the solute in an appropriate solvent to create transparent, single-compound solutions.[7]

Syrup, Elixir and many other liquids are examples of monophasic dose forms.[8]

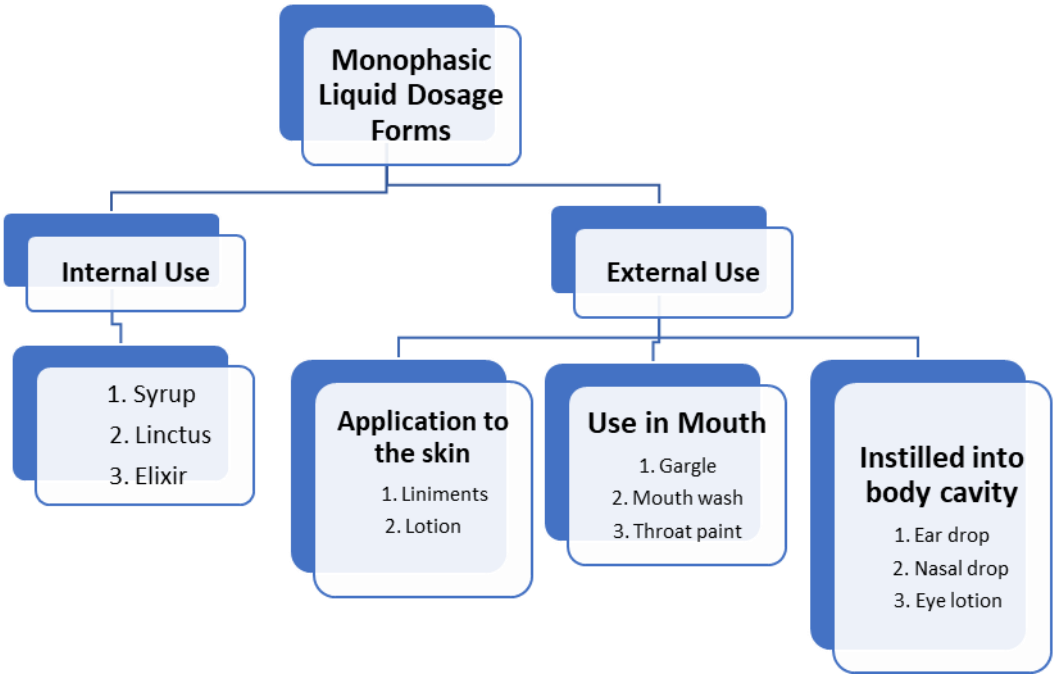

fig. 2: classification of monophasic liquid dosage forms

INTERNAL USE

1.SYRUP:

Syrups are aqueous preparations containing sucrose, in concentrations of sugar 66.7% (w/w), and also contain flavouring agents, and medicinal substances.[9] The simplest type of pharmaceutical preparation that exhibits high absorption of medicinal drugs and rapid onset is a solution.[10]

Types of syrup:[11]

1. Simple syrups: Simple syrups are non-medicated liquid preparations that are primarily used as a medium or vehicle for other liquid medications, providing sweetness and flavour to enhance palatability and facilitate drug administration.
2. Medicated syrups: Medicinal syrups are commonly used for oral administration and may contain various types of medications, including antitussives, expectorants, antihistamines, analgesics, and more.
3. Flavoured syrups: Flavoured syrups are commonly used in the culinary industry to enhance the taste of beverages, desserts, baked goods, and other food items. They come in a wide range of flavours, including popular options like vanilla, chocolate, caramel, strawberry, mint, and more. These syrups can be added to drinks like coffee, tea and cocktails, or used as toppings for ice cream, pancakes, waffles, and other treats.

2.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. However, the majority of linctus comprises chemicals that have expectorant, sedative and antibacterial properties. [12,13]

Linctus is consumed in their concentrated form but not in dilute, so that maximum and prolonged effect can be obtained. For the preparation of linctus, mostly, simple syrups are used as a vehicle and tolu syrup is used for aromatic odour and as a flavour.[14]

3.ELIXIRS:

Elixirs are coloured, aromatic and hydroalcoholic formulations that are sweet in taste but less viscous.[15] Elixirs are transparent and flavoured oral liquids that encompass one or more active pharmaceutical ingredients (API) dissolved in a solution, which typically consists of a substantial concentration of sucrose or suitable polyhydric alcohol.[16]

Elixirs are mainly of two types:[11]

1. Medicinal Elixirs: These are used as solvents or carriers in the manufacture of medicinal elixirs. Dissolve the active ingredient in a 15-50% by-volume ethanol solution:
   a. Elixir (NF)
   b. Compound Benzaldehyde Elixir (NF)

2. Medicated Elixir:
These include:
   a. Antihistamine elixirs for allergies, such as chlorpheniramine maleate (USP) or diphenhydramine hydrochloride
   b. Tranquilizers and hypnotics, the former believed to induce drowsiness and the latter to induce drowsiness
   c. Paediatric elixirs, such as chloral hydrate
   d. Expectorant elixirs, such as pine oil hydrate, for the relief of coughing up phlegm (that is, coughing up phlegm)

EXTERNAL USE:

APPLICATION TO THE SKIN:

1.LINIMENTS

Liniments are topical liquid or semiliquid preparations. These are non-aqueous alcoholic or oily solutions that are applied topically with friction.[17] For the preparation of some liniments, Arachis oil is used as it easily spreads on the skin, comparatively. [18] Drugs that are added in liniments have analgesic, rubefacient, soothing and counter irritant or stimulation properties. It should not be used on the breached or wounded skin as it may cause severe irritation.[19]

Soap is also included as ingredients in some of the liniments which helps in easy application of liniment on the skin.[20]

2.LOTIONS

Lotions are those liquid preparations that are used for topical purposes, applied on the skin without any friction. They can be applied with the help of some absorbent material such as cotton, gauze etc.[21] The medicament used in lotions can be anti-fungal agents like clotrimazole, Eberconazole, etc.[22]

Lotions are applied to the skin's surface with cotton wool for purposes of protection, such as cooling and relaxing. Antiseptic, antibacterial, antifungal, moisturizing and protective substances are prescribed by dermatologists to treat or prevent skin problems.[23]

USE IN MOUTH

1.GARGLE

Gargles are aqueous solutions which are used externally for the prevention and treatment of throat infections. They are prepared in the concentrated form and a direction is mentioned for its use that it should be diluted with warm water prior administration.[24]

The mechanism of gargle is that when it comes in contact with the mucous membrane of the throat and remains in contact for some time, it produces its effect within seconds.[25] Gargles are kept in airtight jar with a plastic screw cover.[26]

2.MOUTHWASH

Mouthwashes are aqueous solutions with a pleasant taste and odour that are used to keep the buccal cavity clean and deodorised. Food particles caught deep inside the throat and mucous in the mouth can be eliminated with the help of mouthwashes with strong flavours and alcohol, which function by producing cough. They come in a variety of flavours, 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. It's primarily used for dental hygiene.[27,28] Generally they contain antibacterial agents, alcohol, glycerine, sweetening agents, flavouring agents and colouring agents.[20]

3.THROAT PAINTS

Throat paints are the viscous liquid dosage form of medicament which are used for the purpose of mouth and throat infections. Glycerine 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.[29]

INSTILLED INTO BODY CAVITY:

1.EAR DROPS

Ear drops are solutions of drugs that are instilled into the ear with a dropper. They are generally used for cleaning the ear, softening the wax and for treating the mild infections.[20]

They are made from water, glycerine, or propylene glycol that are infused into the ear. When viewed under a microscope under suitable conditions of visibility, ear drops are clear solutions that do not include any particles.[30]

2.NASAL DROPS

Nasal drops are sterile liquid preparations containing solutions or suspensions that are administered in nasal cavity with the help of a dropper.[31]

They are usually aqueous and not oily drops. They should be isotonic having neutral pH and viscosity similar to nasal secretions by using methyl alcohol.[20]

3.EYE LOTIONS

Eye lotions are monophasic aqueous preparations intended for eye washing. They are formulated in concentrated form and directed for its use by dilution with warm prior use.[32] It should be free from foreign matter and should be isotonic to avoid unwanted irritation in eyes.[33]

BIPHASIC LIQUID DOSAGE FORM

The liquid which consists of two phases are known as biphasic liquid dosage form. In general both the phases are liquid, while in suspensions the finely divided solids are dispersed in a liquid which acts as a continuous phase.[34]

There are two types of biphasic liquid dosage forms:

- Suspension
- Emulsion

A. 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.[35] The dispersed phase consists of the insoluble or poorly soluble particles for uniform distribution and accurate dosing, while the continuous phase is the liquid vehicle that maintains the stability of the suspension and prevents the setting or aggregation of drug particles.[36] Pharmaceutical suspensions are thermodynamically unstable due to the tendency of solid particles to settle over time. To prevent this, stabilizers or suspending agents are added to the composition.[37] Suspensions are generally taken orally or by parental route. They are also used for external application. Eg. Ampicillin for oral suspensions, Barium sulphate suspensions, Insulin zinc suspensions.[34]

Types of Suspensions: [38,39,40]

1. **According to the Route of Administration:**

a. **Oral Suspensions**: Oral suspensions are intended to be taken by the oral route. To enhance patient acceptability and palatability, suitable flavouring and sweetening agents are commonly added to oral suspensions. These additives help mask the unpleasant taste of the action and make the suspension more enjoyable to consume.
b. **Topical Suspensions**: Topical suspensions are designed for external application, typically on the skin. These suspensions need to be free from gritty particles to ensure a smooth and comfortable application. Gritty particles can cause discomfort, irritation, or potential damage to the skin.
c. **Suspensions:** Parenteral suspensions are administered through injection, typically into the muscle or bloodstream. These suspensions needed to be sterile to prevent the introduction of microorganisms into the body.
d. **Ophthalmic Suspensions:** Ophthalmic suspensions are intended for use in the eyes. They must be sterile to avoid any risk of infection or damage to the delicate ocular tissue. Moreover, ophthalmic suspensions require very fine particles to ensure they can be properly distributed and deliver the active ingredients evenly across the eye surface. Large particles can cause discomfort or interfere with vision.

2. **According to the Nature of the Dispersed Phase and Methods of Preparation**

This classification is based on the type and concentration of solids help in understanding and formulating different types of suspensions for various applications

a. **Dilute Suspensions:** Dilute suspensions contain a relatively low concentration of solid particles, typically ranging from 2-10% weight/volume (W/V). These suspensions are often used for medications where a lower concentration of active ingredient is desired. Eg. Such as cortisone acetate and prednisolone acetate
b. **Concentrated Suspensions:** Concentrated suspensions have a higher concentration of solid particles, usually ranging from 10-50% W/V. These suspensions are used when a higher concentration of active ingredient is needed. Eg. Zinc oxide suspension, which is a concentrated suspension.

3. **According to the nature of sediment**

a. **Flocculated suspension:** In this type, the solid particles of dispersed phase aggregate leading to a network-like structure of solid particles in a dispersion medium. The aggregates form no hard cake.
b. **Non-flocculated suspension:** Non-flocculated suspensions have solid particles that settle slowly and exist separately in the dispersion medium, forming a hard cake. Although they have a more uniform appearance, redispersing the particles may be difficult.

B. EMULSION

The term emulsion is derived from the word emulate meaning “to milk”. An emulsion is a type of biphasic liquid preparation consisting of two immiscible liquids that are dispersed and stabilized with the help of an emulsifying agent.[41] Emulsion contains two phases; one of which is dispersed phase and the other is continuous phase. The liquid is converted into globules minutes which is taken as dispersed phase and the liquid into which the globule is dispersed is known as continuous phase.[42] In normal conditions, the immiscible liquids can’t be dispersed for a long time so for the purpose of stability, emulsifying agent forms a film around the globules so that both the phases can be mixed for a long period of time.[43]

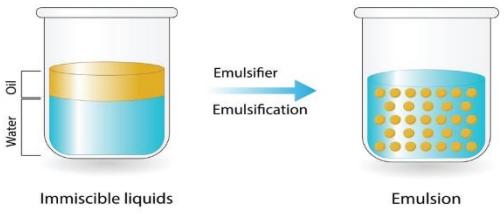

fig. 3: evaluation of emulsion

Types of emulsion:[44,45,46]

1. **Simple Emulsion**: Simple emulsions, also known as primary emulsions that consist of two immiscible fluids: a dispersed phase and a continuous phase. The dispersed phase is usually present as droplets suspended within the continuous phase. Simple emulsions can further be categorized based on the nature of the dispersed phase:

a. **Oil-in-Water (O/W) Emulsion:** In an oil-in-water emulsion, oil droplets are dispersed within a continuous aqueous phase. The oil act as a dispersed phase, and the water acts as a continuous phase. Eg. Milk and most topical lotions.
b. **Water-in-oil (W/O) Emulsion:** In a water-in-oil emulsion, water droplets are dispersed within a continuous oil phase. Water acts as the dispersed phase, and oil acts as the continuous phase. Eg. Butter and mayonnaise.

2. **Multiple Emulsions:** Multiple emulsions, also known as complex emulsions, are emulsions that contain two or more levels of emulsification. They consist of droplets within droplets. Multiple emulsions are designated using a numerical nomenclature (e.g., W/O/W or O/W/O), which indicates the order of the dispersed phases.

a. **Water-in-Oil-in-Water (W/O/W) Emulsion**: In a water-in-oil-in-water emulsion, water droplets are dispersed within oil droplets, which are further dispersed within a continuous aqueous phase. This type of emulsion is used to encapsulate water-soluble compounds within oil droplets. It finds applications in pharmaceuticals, cosmetics and food products.

b. **Oil-in-Water-in-Oil (O/W/O) Emulsion:** In an oil-in-water-in-oil emulsion, oil droplets are dispersed within water droplets, which are further dispersed within a continuous oil phase. This type is used to encapsulate oil-soluble compounds within water droplets. It has applications in controlled release systems and encapsulation technologies.

CONCLUSION

Liquid dosage forms are essential in pharmaceutical therapy due to their rapid onset of action, ease of administration, and flexibility in dosing, especially for children and the elderly. They are classified into monophasic (e.g., syrups, elixirs) and biphasic forms (e.g., suspensions, emulsions), each designed to enhance drug absorption and patient compliance. These formulations often include excipients like sweeteners, preservatives, and stabilizers to improve taste, stability, and shelf life. While they offer significant advantages, such as masking unpleasant tastes and allowing for adjustable dosing, they also have limitations like shorter shelf life, microbial susceptibility, and difficulty in transportation. Despite these challenges, liquid dosage forms remain a critical part of modern pharmacotherapy.

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