ISSN: 2754-5008

Journal of Pharmaceutical Research and Reports

SCIENTIFIC Research and Community

Review Article

Open Access

A Review on Liquid Dosage Form

Lokesh Sharma[1], Vishal Vats[1], Nalin Kaushik[2], Vaishali Saini[1], Sakshi Garg[3], Kaushal Arora[1*] and Prabhakar Kumar Verma[1]

[1]Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, 124001, India

[2]Department of Pharmaceutical Sciences Chaudhary Bansi Lal University, Bhiwani, Haryana, 124001, India

[3]Hindu College of Pharmacy, Sonipat, Haryana, 131001, India

ABSTRACT

Liquid dosage forms are formulations that are administered through oral, parenteral and topical routes. Liquid dosage forms have better patient compliance as compared to other dosage forms hence, mainly used in paediatric patients. Also, during formulation the drugs are uniformly dispensed in liquid dosage form. It masks the taste of bitter, salty and nauseous drugs. This dosage form enhances the drug absorption and in turn, drug bioavailability. During formulation, some non-therapeutic agents (additives) are added that not have any pharmacological potential but still used to enhance the stability, appearance and efficacy of the dosage form to provide better compliance.

***Corresponding author**

Kaushal Arora, Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, Haryana, 124001, India.

Received: June 22, 2023; **Accepted:** June 30, 2023; **Published:** January 31, 2024

Keywords: Additives, Formulation, Liquid Dosage Forms, Patient Compliance

Introduction

Liquid dosage forms are used since past, for rapid and quick absorption of drugs or medicament [1]. This formulation is beneficial for the patients who feel difficulty during intake of solid dosage form (e.g., paediatrics and geriatrics) [2]. Liquid dosage forms are prepared by dissolution of A.P.I (Active Pharmaceutical Ingredients) into a solvent that may be aqueous or non-aqueous which include solutions, suspensions, emulsions etc. The oral route of administration is widely used because of its convenience of self-administration [3].

API or group of APIs can be blended with many excipients such as preservatives, antioxidant, sweeteners, coloring agents, flavoring agents etc. In case of suspensions and emulsions, suspending agents and emulsifying agents respectively, are added for its long-term stability during storage and use [4]. In contrast, liquid dosage forms have an advantage over solid dosage forms as it has no dissolution time and rapidly and efficiently absorbed by GIT [5].

Advantages of Liquid Dosage Forms

- A.P.I is homogeneously dispersed in the formulation.
- Dose can be adjusted by measuring a specific volume.
- Patients having difficulty in swallowing tablets and capsules, can easily swallow solution or syrups e.g., cough syrup.
- Taste of unpleasant drugs can easily be masked by sweeteners and flavoring agents.
- 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.
- Absorbent compounds and antacids can be easily administered via liquid dosage form.
- Some hygroscopic and deliquescent compounds that release water during solid formulations can be easily dispensed through liquid dosage forms.
- The therapeutic response is faster than solid dosage form [6].

Disadvantages of Liquid Dosage Forms

- Liquid is comparatively difficult during handling and storage.
- The shelf life is less in liquid dosage forms.
- Ingredients are usually more susceptible to degradation.
- Two incompatible components can't be dispensed together as compared to solid dosage forms.
- Inconvenient for travelling purposes as there is a problem of spillage.
- Solutions are quickly degraded by microorganisms therefore; preservatives are intended to be added into the formulations [7].

Types of Liquid Dosage Forms

Monophasic Liquid Dosage Forms

Monophasic liquid dosage forms has only one phase.

Syrups

Syrups are defined as the concentrated solution in which sucrose is dissolved in purified water. They are sweet in taste and highly viscous. In simple syrups, the sucrose concentration is 66.7% (w/w) [8]. They are classified as

Medicated Syrups

Syrups that contain medicament.

Non-Medicated Syrups
Syrups that are made only for flavoring purpose.

Elixirs
Elixirs are colored, aromatic and hydroalcoholic formulations that are sweet in taste but less viscous. These solutions are formulated by adding ethyl alcohol, water, flavoring agents, syrups and preservatives [9]. Variety of medicated formulations are present in market which contains very potent therapeutic agents like antibiotic elixirs, antihistaminic elixirs, sedative elixirs. Sometime flavoring elixirs are used for flavors as well as vehicles for further formulations [10].

Linctus's
Linctus is concentrated oral preparations used for the treatment of cough. The API used to prepare linctus are demulcents, sedatives and expectorants [11]. 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 odor and as a flavor [12].

Drops
Drops are liquid preparation used for the oral administration. Some vitamins such as vitamin A and vitamin D that are water insoluble but are oil soluble are dispensed in the form of drops for better administration. During administration, the dose can be accurately measured, hence, commonly used in pediatric formulation [13].

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 material such as cotton, gauze etc [14]. They are applied for the treatment of skin related diseases. The medicament used in lotions can be anti-fungal agents like clotrimazole, Eberconazole, etc. It provides cooling, soothing and protective effect, etc [15].

Liniments
Liniments are topical liquid or semiliquid preparations. These are non-aqueous alcoholic or oily solutions that are applied topically with friction. Alcohols increase the counter-irritant action and drug penetration into the skin [16]. For the preparation of some liniments, Arachis oil is used as it easily spreads on the skin, comparatively [17]. Drugs that are added in liniments have analgesic, rubefacient, soothing, and counter irritant or stimulation properties. They should not be used on the breached or wounded skin as it may cause severe irritation [18].

Gargles
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 [19]. 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 [20].

Throat Paints
Throat paints are viscous and liquid formulations used for the treatment of infections of mouth and throat. In this preparation glycerin is taken as a base. They are sweet in taste [21].

Nasal Drops
Nasal drops are sterile liquid preparations containing solutions or suspensions that are administered in nasal cavity with the help of a dropper [22]. Aqueous drops are preferred instead of oily drops. Ideally it should have neutral pH and its viscosity must be similar to the nasal secretions and should be isotonic [23].

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 water prior use [24]. It should be free from foreign matter and should be isotonic to avoid unwanted irritation in eyes [25].

Eye Drops
Eye drops are sterile preparations containing solutions or suspension of API that is administered in the eye with help of a dropper [26]. It is prepared with aqueous vehicle and be isotonic with secretions of lachrymal gland and free from any foreign matter to prevent unwanted irritation [27].

Biphasic Liquid Dosage Forms
It consists of two phases:
For example: Suspension and Emulsions

Suspensions
Suspensions are biphasic liquid dosage form in which medicament is finely divided into small solid particles that easily gets dispersed in a liquid vehicle. It contains two phases; one of which is dispersed phase and the other is continuous phase [28]. Solid particles behave as dispersed phase while vehicle as continuous phase. Suspensions can be administered through oral or parenteral route as well as used for external purposes [29]. Example: Amoxicillin oral suspension, Insulin Zinc suspension.

Emulsions
Emulsions are biphasic liquid dosage form consisting of two non-miscible liquids i.e., oil and water. Emulsion contains two phases; one of which is dispersed phase and the other is continuous phase [30]. 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 [30]. In normal conditions, the immiscible liquids can't be dispersed for a long time so for the purpose of stability, emulsifying agents are added into the emulsion system. Emulsifying agent forms a film around the globules so that both the phases can be mixed for a long period of time [31].

Emulsions are Classified as
Oil in Water type (O/W)
Water in Oil type (W/O).
Multiple emulsions (O/W/O or W/O/W).

Formulation of Liquid Dosage Forms
Excipients
Excipients are the compounds other than active ingredient that are used in the formulation of any dosage form. Excipients are commonly inactive and don't have any therapeutic value but still needed for the preparation of dosage form [32]. They are inert in nature and not have any therapeutic or pharmacological effect. They can be derived from natural or synthetic source that are included into a formulation for following prospects as:

- It increases the stability of the dosage form
- Mask the bitter taste of drugs
- Provides flavor and color to the formulation etc.

Liquid dosage form includes solution, suspension and emulsion that are formulated depending upon the nature of active ingredient as well as its solubility and stability [33]. They are also designed as ready to use liquids, as after reconstitution into to liquid and such as syrup, solution, suspension and emulsions. In the liquid formulation many types of excipients are added such as stabilizer, sweeteners and flavoring agents etc [34]. Its selection also plays an important role for the designing of flavoring and effective dosage forms [35].

Selection of Excipients

Selection of excipients are totally dependent on physical and chemical properties, characteristics of drug constituents, dosage forms and on the route of administration [36]. The major concern in development of oral liquid dosage form is active pharmaceutical ingredients. Following are some major challenges occur during development of liquid dosage forms:

- Drug stability in solution.
- Drug solubility at a required level.
- Effective taste.

The compatibility of excipients in solution account for the same as the compatibility of recipients with a solid-state drug [37]. If the mechanism of degradation is known then the process of selecting a suitable excipient will be easier. To choose a proper excipient, drugs physicochemical properties like pH stability and Pka value should be known [38].

Ideal Properties of Excipients are as Follows

- It should have efficient functionality.
- It should have physicochemical stability.
- It must be inert and non-toxic in nature.
- It should not be sensitive with equipment's and machineries.
- It should be easily available and economically effective [39].

Functions of Excipients

- For the maintenance of integrity in the dosage form excipients are added.
- Excipients make up the enough volume of the formulation for its proper handling and administration.
- Excipients provide acceptance to the patient, for example by including flavoring agent.
- It enhances the bioavailability of the drug.
- It provides assistance to the patients [40].

Excipients Used in Formulation of Liquid Dosage Forms

Oral liquid dosage form needs a combination of ingredients of different concentrations that perform various functions like solubilization, provides suitable colors, sense of taste and viscosity [41]. Excipients must be compatible and inert and should be stable for a desired period. There are some common excipients that are generally used in preparations like base (vehicle) that may be aqueous or non-aqueous, viscosity builders that enhances viscosity, preservatives that prevent microbial growth, coloring agents that provide elegant appearance to the formulation, flavoring agent that provide flavor like orange tincture, suspending agents used in the formation of suspensions, emulsifying agents used in case of emulsions [42].

Vehicle

Vehicles are also known as base pharmaceutical formulations in which the active pharmaceutical ingredient and other excipients are dissolved. Vehicle are of two types:

- Aqueous vehicles: water is a common example of aqueous vehicle, commonly used in case of syrups.
- Non-aqueous vehicles: also known as oily vehicles, for example vegetable oils and organic oils as emulsified bases.

Water

Distilled water and purified water obtained by distillation process or any other suitable process are used in the formulation. The water that obtained from nature have so much dissolved impurities [43-44]. Some inorganic impurities that are dissolved in natural water are potassium, calcium, magnesium, sulphates and bicarbonates but some organic components are barely soluble or maybe present in insoluble state. Microorganisms are also present in natural water and the microbial load in natural water is known as bio-burden [45]. Generally, water for drinking contains less than 0.1% solids. However, drinking water is not preferable for pharmaceutical formulation. United States pharmacopoeia (USP) permits the use of purified water as a vehicle or an element of aqueous formulations instead of parenteral preparations (injections). To obtain purified water suitable processes like distillation, ionexchanger's (Reverse Osmosis) are used [46].

Alcohol (Ethyl Alcohol)

It is well known solvent for the preparation of pharmaceutical products or dosage forms. In pharmaceutical field, alcohol is the second most useful solvent after water [47].

Glycerol

It is also known as glycerin. It is a clear, colorless and viscous liquid that provides oily sensation during touch. It is sweet in taste, when exposed to air it absorbs the moisture i.e, hygroscopic in nature [48]. It is prepared by the decomposition of animal fats and vegetables and contains approx. 95% of absolute glycerin. It is soluble in all proportions of alcohol as well as in water but not soluble in ether, chloroform, benzene. It is used to prepare various pharmaceutical products such as elixir of phosphoric acid, syrups and tinctures [49].

Propylene Glycol

Propylene glycol play a variety of roles as an extractant, solvent and preservatives in parenteral and non-parenteral pharmaceutical preparations [50].

Preservatives

Contamination of pharmaceutical products by microorganisms is a major problem in aqueous based liquid dosage forms. Preservatives inhibit the growth of microorganisms. Ideally, preservatives must be compatible, effective at lower concentration against possible microorganisms, should be non-toxic and non-reactive with various components of the formulation. They should be stable during the shelf life of the preparations [51].

Most of the preservatives are bacteriostatic in action and can be acidic and non-acidic. Acidic type of preservatives include phenol, benzoic acid, boric acid, and their related salts [52]. Some other neutral preservatives include benzyl alcohol and β-phenyl ethyl alcohol. Preservatives consist of reactive functional groups that has antimicrobial potential but these functional groups led to some unwanted reactions [53].

Antioxidants are efficient excipients that prevent the oxidation of compounds. The impurities that are present in active pharmaceutical ingredients or in excipients act as catalyst for oxidation reactions. Most of the drugs exist in reduced form that's why they are highly unstable [54]. Drugs that contain phenolic and sulfhydryl group are affected by oxidation because the drug in the ionized form

participates in oxidation [55]. E.g., Adrenaline, the only compound that slowly oxidized at pH less than 4 but quickly destroys under alkaline pH conditions. They inhibit the chain reaction with free radicals in the formulation and inhibit free radical propagation cycle. Antioxidants are mixed with chelating agents and the combination produce synergistic effect because these agents act at different steps in oxidative process [56]. Examples: acetone, sodium bisulfite, acetyl cysteine, ascorbic acid, thiourea.

Flavoring Agents

Flavors are mixture of sensations of taste and flavors and involves the blend of physicochemical and physiological actions of substance. Ideally the flavors that are used in the formulation must be nontoxic in nature, properly soluble in the preparation and should be compatible with the liquid formulation [57]. Some flavors that are sweet in nature increases the blood sugar level that may cause harmful effects in the diabetic patients so in those cases, artificial flavors are used. In the aqueous liquid preparation water soluble flavors are added on the other hand, poorly water-soluble flavors are added into non aqueous preparations [58].

Sucrose is an example of sweetening agent. It enhances the thickness of the liquid and also provides a pleasant texture in the mouth [59]. Sucrose causes harmful effect in diabetic patients so, alternate of sucrose, artificial sweetening agents such as sorbitol, saccharine etc. are used in food and pharmaceutical products. These artificial sweeteners faced some challenges over the safety by FDA and instructions in their uses and sales effect in 1969. Sucralose is one of the most popular compounds used as sweeteners due to its excellent sweetness and also a low-calorie compound but it is expensive [60].

Colorants

Coloring agents are those compounds which provide a color to the formulation. Colors that are used in the liquid dosage form should be certified by FDA as per D&C Act 1940. Some colorants like Sulphur (yellow), riboflavin (yellow), cyanocobalamin (red), ferrous sulphate (bluish green) is of natural origin but not used in pharmaceutical formulations [61]. Now a days, most of the synthetic colors are used in the formulation but some natural minerals and plant source such as red ferric oxide when compounded with zinc oxide powder gives calamine color i.e., characteristic of the skin tone. During selection of the colorant, age of the patient plays an important role because it seems that certain age group prefer certain colors as children prefer a sweet and fruity flavor [62].

Wetting Agents and Surfactants

Wetting agents are used in pharmaceutical formulation for the routine purposes, and especially used in liquid dosage form to create a homogeneous mixture of solid into liquid vehicle. Wetting process are challenging process due to absorption of air particles on the solid particles surface. Until the air not completely displaced, the solute particles float on the surface of the solvent and at that time the wetting agent remove the air and easily penetrates the liquid into the surface [63]. Aqueous vehicles such as alcohol and glycerol commonly used for the removal of absorbed air from the surface of solid particles but for non-aqueous vehicles mineral oil is frequently used as wetting agents. Surface active agents are those compounds which reduce the non-aqueous interfacial tension. Most commonly used examples of surfactant are "sodium lauryl sulphate". The (HLB) Hydrophilic-Lipophilic Balance value of wetting agents exists between 7 and 9 [64].

Buffering Agents

Buffering agents are also known as pH modifier. The pH plays a key role in liquid formulations. These are used to prevent the variation of pH in the formulation that also prevents a large number of changes during storage. The concentration of the buffering agent is sufficient between 0.05M and 0.5M. The suitable buffer can be selected on the basis of the drug stability and excipients in the buffer, compatibility of container and buffers [65].

In most of the cases combination of buffers as compared to individual buffer are used to gain wider ranges of pH. Not all types of buffers are suitable for every preparation, for example boric acid buffer can be used in the preparation of optical and parenteral fluids but not used for oral liquids because of its toxic effect. Solubility of excipients are influenced by the buffers. Some commonly used buffers are carbonates, citrates and tartrates [66].

Suspending Agents

The selection of an ideal suspending agent for the formulation of suspension is also a critical factor which is based on viscosity and the settling time of particles. Other factors that are considered during selection of an ideal suspending agents are its rheological properties, suspending capacity in the formulation, compatibility with other excipients and economically effective. Examples of suspending agents are natural gums, synthetic gums etc [67].

Flocculating Agents

Flocculating agent prevents the caking of suspension. The solid particles that are dispersed in formulation causes setting down and form a solid cake of substance in the bottom of the container, so to prevent this condition, the flocculating agents are used [68]. Some examples of flocculating agents are starch, sodium alginate etc.

Chelating Agents

Chelating agents are those that form chelates with metal ions causes activation of their catalyst property in oxidation. These agents have a property of formation of complex with the drugs that are involved in complex compound containing two or more bond and rings in its structure. It protects the API from catalysts that plays a role acceleration in oxidation reactions [69].

Emulsifiers

Emulsifiers are the compounds that reduce the interfacial tension between the two immiscible liquids, usually water and oil and form a barrier around both the droplets of the immiscible liquids. Emulsifiers contain hydrophilic and lipophilic portions [70].

The ideal properties of emulsifying agents are as follows: they should be nontoxic, economically effective, should not have any harmful effect on body, should not have any therapeutic effects, must be stable to chemical degradation. Some of the examples of emulsifiers are: acacia, stearic acid, lecithin, lanolin alcohols etc [71].

Conclusion

Liquid dosage forms are widely accepted by patients due to better compliance. There are numerous additives are discovered and developed to conquer the limitations of existing marketed liquid dosage forms. But still there are more need to develop more effective and efficient liquid dosage forms for more patient compliance and increased bioavailability.

Author's Contribution

LS and KA researched and wrote this review. NK, VS, SG and VV design it. PKV provided guidance, critical review and revision of the manuscript. All authors read and approved the final manuscript.

References

1. SV Sastry, JR Nyshdham Fix (2000) Recent technological advances in oral drug delivery a review, Pharmaceutical Science and Technology Today 138-145.
2. H Seager (1998) Drug-delivery products and the Zydis fast-dissolving dosage form, Journal of Pharmacy and Pharmacology 50: 375-382.
3. Vats V (2020) Novel Drug Delivery System: Resealed Erythrocytes. Turkish Journal of Computer and Mathematics Education (TURCOMAT) 11: 706-719.
4. Chang Dorothy, Chang Ron Kun (2007) Review of current issue in pharmaceutical excipients, available on https://www.pharmtech.com/view/review-current-issues-pharmaceutical-excipients
5. Pramod Lakshmana, KS Reddy, JD Reddy, SG Vasantharaju (2010) Global regulatory perspective of bulk pharmaceutical excipients. Manipal Academy of Higher Education 8.
6. J Patrick Crowley, G Martini Luigi (2006) excipients for pharmaceutical dosage forms, Encyclopedia of pharmaceutical technology www.informaworld.com.
7. Vats V, Kunal AD, Dhiman S, Singla C, Sharma A (2020) A Review on Marketed Herbal Formulations with Immuno-Modulating Potential. Elementary Education Online 19: 3079-3099.
8. Ashok Katdare, Mahesh V Chaubal (2006) Excipient development for pharmaceutical biotechnology and drug delivery systems, Informa Healthcare USA 1-2.
9. Giorgio Pifferi, PatriziaRestan (2003) the safety of pharmaceutical excipients, farmaco 58: 541-550.
10. White AR (2015) The Success of Solanezumab Should Drive Renewed Efforts to Develop Small Molecule Anti-Amyloid Agents for Alzheimer's disease Therapy. Drug 4: e128.
11. Gomase VS, Kale KV (2015) Information of Surface Accessibility of the Peptide Fragments of Coat Protein from Alfalfa mosaic virus (AMV) at the Physicochemical and Immunochemical Levels. Drug Des 4: 1-119.
12. Bule MH, Haymete A, Kefale B (2015) Synthesis and In-Vivo Pharmacological Evaluation of Some Novel 4(3H)-Quinazolinone Derivatives as Potential Anti-malarial Agents. Drug Des 4: 1-121.
13. Yuh-Jenn Wu, Chi-Tian Chen, Hsiao-Hui Tsou, Chin-Fu Hsiao (2015) Evaluating the Relative Cost of a Targeted Design versus an Untargeted Design for Randomized Clinical Trials. Drug Des 4: 1-120.
14. Pharmacopoeia European, (2005) "5.0 liquid preparation for oral use", EDQM— European Directorate for the quality of medicines, Strasbourg, France, (609), 5th edition. https://www.edqm.eu/en/
15. Chow SC, Pong A (2014) Statistical Designs for Pharmaceutical/Clinical Development. Drug Des 3: 1-112.
16. Vaidya (2014) Drug Designing and Development: Emerging Role of Health Technology Assessment. Drug Des 3: 1-111.
17. Toshihiko Tashima (2014) Multifunctionality of Drug's Pharmacophores within an Organism. Drug Des 3: 1-116.
18. Chow SC, Chiu ST (2013) A Note on Design and Analysis of Clinical Trials. Drug Des 2: 1-102.
19. Nayak UY (2013) Role of Nano-Particles in Drug Therapy-Drug Delivery Approach. Drug Design S5: e001.
20. Nirmala MJ, Nagarajan R (2016) Microemulsions as Potent Drug Delivery Systems. J Nano medNanotechnology 7: 1-139.
21. AbouAitah KEA, Farghali AA, Swiderska-Sroda A, Lojkowski W, Razin AMF, et al. (2016) pH-controlled Release System for Curcumin based on Functionalized Dendritic Mesoporous Silica Nanoparticles. J Nano medNanotechnology 7: 351.
22. Patil JS (2016) Significance of Particulate Drug Delivery System in Antimicrobial Therapy. Adv Pharmacoepidemiology Drug Saf 5: 139.
23. Dudhipala N, Narala A, Janga KY (2016) Amoxycillin Trihydrate Floating-Bio adhesive Drug Delivery System for Eradication of Helicobacter pylori: Preparation, In Vitro and Ex Vivo Evaluation. J BioequivAvailable 8: 118-124.
24. Naydenov T, Stoimenova A, Kassarova M (1994) Opinion of Bulgarian Pharmacists on Drug Delivery Systems, Or dispersible and Pediatric Dosage Forms. J App Pharm 8: 1-211.
25. Agathe Wehrli (1994) The Pharmaceutical Codex Principles and practice of Pharmaceutics 12: 189.
26. Coelho M (1991) Fate of Vitamins in Premixes and Feeds: Vitamin Stability. Feed Management 42: 22-24.
27. Akhtar MJ, Khan MA, Ahmad I (1999) Photodegradation of folic acid in aqueous solution. J Pharma Biomed Anal 19: 269-756.
28. Ekinci R, Kadakal C (2005) Determination of seven water-soluble vitamins in Tarhana, a traditional Turkish cereal food, by High-Performance Liquid Chromatography. ActaChromatographica 15: 289-978.
29. Deshpande SW, Nilesh G (2000) Drugs and Cosmetics Act 1940 and Rules 1945 2Edn 538-539.
30. Nelson DH, Samuels LT (1952) A Method for Determination of 17-Hydroxycorticosteroids in Blood: 17-Hydroxycorticosterone in the Peripheral Circulation. J Clin Endocrinol &Metab 12: 519.
31. Glenn EM, Nelson DH (1953) Chemical Method for the Determination of 17-Hydroxycorticosteroids and 17-Ketosteroids in Urine Following Hydrolysis With β-Glucuronidase. J Clin Endocrinol & Metab 13: 911.
32. Bayliss RES, Steinbeck AW (1953) A Modified Method for Estimating 17-Hydroxycorticosteroids in Plasma. BiochemJ 54: 523-527.
33. Pal V,Nahata M(2001) Need for extemporaneous formulationsin pediatric patients. J Pediatric Pharmacotherapy 6: 107-119.
34. Joseph FS, Catherine Tuleu (2005) Pediatric Formulations-Getting to the heart of the Pediatric of Pharmaceutics 300: 56-66.
35. Standing JF, Khaki Z F, Wong I (2005) Poor formulation information in published pediatric drug trials. Pediatrics 116: 559-62.
36. Alexander KS, Haribhakti RP, Parker GA (1991) Stability of acetazolamide in suspension compounded from tablets. Am J Hosp Pharm 48: 1241-44.
37. Fawcett JP, Stark G, Tucker IG, Woodd DJ (1994) Stability of dantrolene oral suspension prepared from capsules. J Clin Pharm Ther 19: 349-53.
38. Anonymous (2000) Boots pharmacist and trainee cleared of baby's manslaughter. Pharm J 264: 390-92.
39. Burton RB, Zaffaroni A, Keutmann EH (1951) Paper Chromatography of Steroids. II. J Biol Chem 188:763-71
40. ALEJANDRO ZAFFARONIt, ROBERT B BURTON (1951) Corticosteroids and Related Compounds. J Biol Chem 1951 188-763.
41. Nelson DH, Sandberg AA, Palmer JG, Tyler FH (1952)

Blood Levels of 17-Hydroxycorticosteroids Following the Administration of Adrenal Steroids and Their Relation to Levels of Circulating Leukocytes. J Clin Invest 31: 843.

42. Stewart PJ, Tucker IG (1982) A survey of current extemporaneously prepared pediatric formulations. Aust J Hosp Pharm 12: 64-68.
43. Tan E, Cranswick NE, Rayner CR, Colin B Chapman (2003) Dosing information for pediatric patients are they really therapeutic orphans Med J Aust 179: 195-198.
44. Mihaila B, Ellis D, Rozek T, Milne R (2012) Chiral Stability Study of Oral Liquid Clopidogrel Formulations for Infants. J Pharm Prac Res 42: 106-110.
45. Walker SE, Baker D, Law S (2005) Stability of clozapine stored in oral suspension vehicles at room temperature. Can J Hosp Pharm 58: 279-284.
46. Walker SE, Baker D, Law S (2005) Stability of clozapine stored in oral suspension vehicles at room temperature. Can J Hosp Pharm 58: 279-284.
47. Chou J, Decarie D, Dumont RJ (2001) Stability of dexamethasone in extemporaneously prepared oral suspensions. Can J Hosp Pharm 54: 97-103.
48. Cober MP, Johnson CE, Sudekum D, Penprase K (2001) Stability of extemporaneously prepared glycopyrrolate oral suspensions. Am J Health Syst Pharm 68: 843-845.
49. Ensom MH, Decarie D, Sheppard I (2007) Stability of lansoprazole in extemporaneously compounded suspensions for nasogastric or oral administration. Can J Hosp Pharm 60: 184-191.
50. Melkoumov A, Soukrati A, Elkin I, Forest JM, (2011) Quality evaluation of extemporaneous delayed-release liquid formulations of lansoprazole. Am J Health Syst Pharm 68: 2069-2074.
51. Ensom MH, Decarie D, Rudolph S (2011) Stability of levetiracetam in extemporaneously compounded suspensions. Can J Hosp Pharm 64: 207-211.
52. Johnson CE, Cober MP, Thome T, Rouse E (2011) Stability of an extemporaneous alcohol-free melatonin suspension. Am J Health Syst Pharm 68: 420-423.
53. Aliabadi HM, Romanick M, Somayaji V, Mahdipoor P, Lavasanifar A (2011) Stability of compounded thioguanine oral suspensions. Am J Health Syst Pharm 68: 900-908.
54. Anderson, Meagan Opawale, F Rao, M Delmarre, D Anyarambhatla, Gopal (2006) Excipients for Oral Liquid Formulations 1-20.
55. LH Reddy, B Ghosh, Rajneesh (2002) Fast dissolving drug delivery systems a review of the literature Indian Journal of Pharmaceutical Science 64: 331-336.
56. M C Gohel (2005) A review of coprocessed directly compressible excipients, j.pharmpharmaceut sci 8: 26-93.
57. A Modi, P Tayade (2006) Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS Pharm Sci. Tech 7: 68-75.
58. Hans Leuenberger (2006) Functionality excipients towards drug carrier system, Chimi Caoggi. Chemistry today 24: 64-66.
59. Loyd V, Nicholas, Allen, Popovich G, Howard C (2006) pharmaceutical dosage forms and drug delivery systems, eighth edition, Indian edition, B.I Publications pvt ltd 342-343.
60. Rowe R C, Sheskey P J, Weller P J (2003) Handbook of Pharmaceutical Excipients, Fourth Edition, Pharmaceutical Press, London, United Kingdom, and the American Pharmaceutical Association, Washington, DC 1-917.
61. G Mosher, D Thompson (2000) Complexation and cyclodextrins In J. Swarbrick and J C Boylan (eds.), Encyclopedia of Pharmaceutical Technology 19: 49-88.
62. M J Akers (2002) Excipient-drug interactions in parenteral formulations. J Pharm 91: 2283-2306.
63. R C Fu, D M Lidgate, J L Whatley, T McCullough (1987) The biocompatibility of parenteral vehicles-in vitro/in vivo screening comparison and the effect of excipients on hemolysis. J Parent Sci Technol 41: 164-168.
64. M Radwan (1994) In vivo screening model for excipients and vehicles used in subcutaneous injections Drug Dev. Ind Pharm 20: 2753-2762.
65. D Thompson, D M V Chaubai, (2002) Cyclodextrins (CDS)-excipients by definition drug delivery systems by function (part I: injectable applications) Drug Delivery 2: 34-38.
66. M L Chen (2002) Lipid based oral dosage forms-regulatory perspective Am. Pharm. Rev 5: 30-35.
67. D J Hauss (2002) Lipid-based systems for oral drug delivery enhancing the bioavailability of poorly water-soluble drugs. Am. Pharm. Rev 5: 22-36.
68. C J H Holm, A Porter, H G Kristensen, W M Charman (2002) Structured triglyceride vehicles for oral delivery of halofantrine examination of intestinal lymphatic transport and bioavailability in conscious rats. Pharm. Res 19: 1354-1361.
69. W Curatolo (1998) Physical chemical properties of oral drug candidates in the discovery and exploratory development settings. Pharm Sci Tech 1: 387-393.
70. Ansel, H C, Allen, L V, Popovich, N G (2006) Pharmaceutical Dosage Forms & Drug Delivery Systems, 8th ed, Lippincott Williams & Wilkins 121-145.
71. Aulton M E (2002) Pharmaceutics -The Science of Dosage Form Design 113-138.
72. Gaud R S, Yadav A V, Gokhale S B (2007) Textbook of Pharmaceutics, 10th Ed, Nirali Prakashan, New Delhi. 102-135.