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Pharmaceutical Jellies: A novel way of drug delivery

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Abstract

Oral route of drug administration is the most convenient and acceptable route gaining more patient acceptance. But the main problems of oral drug delivery system involves unpleasant or bitter taste of the formulation, difficulty in swallowing and low bioavailability.

While considering paediatric population the main problem is at what age children can safely swallow an oral medication especially tablets and capsules. Jellies can be easily swallowed even by children who does not have their primary teeth. For any paediatric formulation taste, colour, flavour, texture and its acceptance are very important. Children are unlikely to tolerate the repeated administration of any drugs and this becomes a major issue for the parents who are trying to administer the medicaments.

The best way to solve these problems are formulating a paediatric friendly dosage form which will be more acceptable among children in its taste, smell, colour, texture. It has estimated that about 50% of population has problem of swallowing tablets especially paediatrics and geriatrics[5]. Jellies are the most suitable dosage form for even dysphagia patients.

Keywords: Pharmaceutical jellies, paediatric formulation, dysphagia, geriatrics, bioavailability

INTRODUCTION

Patients are usually comfortable with oral drug delivery system since it is non-invasive and usually offers low cost of treatment. Also the safety, efficacy and cost effectiveness of oral drug delivery system enhances its patient compliance.

Current paediatric formulation have so many drawbacks. Most of the paediatric formulations available in the market are tablet, capsules, syrups, solutions and drops. For liquid formulations dose volume is a major consideration.[3] Only dose volume less than 5ml is recommended for children under five years and less than 10ml is recommended for children of five years and older.

Stability issues of liquid formulations are another concern. The drug is being in solution or suspension form and easy for its degradation. We know that API of majority of the drugs are bitter in taste[1]. Since the drug is completely or partially dissolved in it and when get into direct contact with the taste receptors of the tongue, it becomes an unacceptable formulation especially for children. Also these formulations requires higher amount of sugar or other sweeteners in high concentration for taste masking. Here also jellies can overcome this problem since jellies are having high viscosity. This property can be utilised for taste masking, solving stability issues and enhancing sustained release. Controlled release jellies are also practical by controlling the viscosity of polymers or embedding controlled release delivery system.

Chewable dosage forms are more convenient in administration of drugs for dysphagia patients and offers ease of handling compared to liquid and powder formulations. Chewable formulation has high drug carrying capacity and requires less amount of super disintegrants. Aesthetic appearance and pleasing taste of soft chewable system easily attracts children.

JELLY

17th edition of Japanese Pharmacopeia[1] defines jellies meant for oral administration as non- flowable gelatinous preparations of definite size & shape, meant for oral administration. Jellies can be defined as semisolid preparations that are transparent, translucent or nongreasy, intended for internal or external application. The sources from which jellies can be prepared are natural gums like tragacanth, pectin, sodium alginates or from synthetic derivatives like methyl cellulose and sodium carboxy methyl cellulose. As these jellies have eye catching appearance, pleasant taste and easy to handle, everyone prefers jelly over oral liquids or tablets. Medicated jelly can be utilised for the local treatment of ailment related to oral cavity & as well as systemic condition. Oral medicated jellies are palatable solid dosage forms administered in the oral cavity, meant to be dissolved in mouth or pharynx for its local or systemic effect.

By using pharmaceutical jellies as dosage form, drug delivery through buccal route, labial route, gingival route and sublingual routes are possible. For chronic illness treatments multiple drugs can also be incorporated in them. Pharmaceutical jellies are now available as otc medicaments in different flavours containing drugs for anaesthetics, erectile dysfunction, arthritis, antihypertensive, sore throat. Jellies can be used as a choice for psychiatric and patients suffering from stroke, thyroid disorder, Parkinson's diseases and multiple sclerosis, nausea, vomiting and motion sickness. Patients for whom chewing is difficult, painful or lower jaw is paralyzed can use medicated jellies easily. Jellies can be used easily in children who have lost their primary teeth but do not have full use of their permanent teeth. Medicated jellies are able to release drug in the mouth and for absorption passed through local oromucosal tissues and through pre-gastric, gastric and post gastric segments of

the gastrointestinal tract.

European Medicines Agency considers the following criteria for an ideal paediatric formulation[3]

- Dosage frequency must be minimum
- One dosage form fits all or a full range
- Minimal impact on life style
- Minimum, non-toxic excipients,
- Convenient, easy, reliable administration,
- Easily produced, elegant, stable,
- Cost and commercial viability.

Ideal Characteristics of Oral medicated jellies

- It should leave minimal or no residue in mouth after oral administration, compatible with pleasing mouth feel.
- Be compatible with taste masking.
- Effective taste masking technologies should be adopted for bitter taste drugs.
- Be portable without fragility concern.
- Leave negligible or no residue in the mouth after oral administration.
- Variations towards changes in environmental conditions should be less.
- Allow high drug loading.
- Adaptable and amenable to conventional processing and packaging equipment at nominal expense.
- The drug and excipients property should not affect the orally disintegrating tablet.

Advantages of jelly

- It can be administer easily i.e., anywhere, anytime as it is easy to handle & doesn't require water.
- Therapeutic action of drug can be terminated by spitting it before complete ingestion of medicated jelly
- It can also be used for systemic delivery of drugs, which are prone to metabolism in the gut wall or liver.
- Moreover the drugs that are liberated & swallowed from medicated jelly, will reach the gastrointestinal tract either in dissolved or suspended form in saliva and hence it will be easily available.
- Delivery of therapeutic agent to systemic circulation through the oral mucosa can help to overcome the problems related to difference in drug release and retention times.
- It serves as ideal method of drug delivery for dysphasia patients as it reduces the risk of aspiration
- Pharmaceutical jellies can be administer to the patients who cannot swallow tablets or capsules such as the elderly, stroke victims, bedridden patients, patients with esophageal problems & patients who refuse to swallow such as paediatric, geriatric
- & psychiatric patients and thus improves patient compliance.
- As saliva pass down it facilitate rapid absorption of drugs through pre-gastric absorption from mouth, pharynx & oesophagus and increases bioavailability.
- Jelly is most convenient for disabled, bedridden patients, travellers and busy people, who do not always have access to water.
- Good mouth feel property of jellies helps to change the perception of medication.
- While administering conventional oral dosage form there is a chance of choking and by using jellies safety can be assured.
- Pharmaceutical jellies opened new business opportunity like product differentiation, product promotion, patent extension and life cycle management.
- Suitable during traveling where water may not be available.
- Conventional manufacturing equipment.
- Cost effective.
- Good chemical stability as conventional oral solid dosage form.
- Allow high drug loading.
- Provides rapid drug delivery from dosage forms.
- Adaptable and amenable to existing processing and packaging Machinery.
- Rapid onset of action.
- It is convenient to administer – anywhere, anytime, doesn't require water.
- The treatment can, if required, be terminated at any time.
- It may prove to be particularly suitable for the systemic delivery of drugs, which are susceptible to metabolism in the gut wall or liver.

In addition, the drugs that are released from jelly and swallowed, will be introduced in the gastrointestinal tract either dissolved or suspended in saliva and thus will be present in readily bioavailability form.

CLASSIFICATION OF JELLIES[10,11]

Jellies can be classified as

a) Medicated Jelly

These are mainly used over mucous membrane and skin & they possess spermicidal, local anaesthetics, and antiseptic properties. These jellies hold adequate amount water which after evaporation gives a local cooling effect and residual film provides protection Example: Ephedrine sulphate jelly is used to seize the bleeding of nose since it is vasoconstrictor.

b) Lubricating Jelly

These jellies are intended for lubrication of equipments used in diagnosis like surgical gloves, catheters, cystoscopes

c) Miscellaneous Jelly

These are intended for diverse applications like electrocardiography & patch testing.

Challenges in Formulating Oral medicated jellies[13]

- Palatability

Masking taste of bitter drugs and enhancing taste directly related to patient compliance.

- Hygroscopicity[14]

Some oral jelly dosage forms are hygroscopic and they need protection from humidity so needs specialized product packaging.

- Dose /Amount of drug

When the drug possess bitter taste, more excipients should be added to mask taste and this in turn increases the final size of dosage form

- Aqueous solubility[15]

Various excipients in jelly imparts crystallinity and rigidity for water soluble drugs which forms eutectic mixtures.

- Size of jelly

The degree of ease in taking a jelly depends on its size. It has been reported that the easiest size of jelly to swallow is 78mm while the easiest size to handle was one larger than 8 mm. Therefore, the jelly size that is both easy to take and easy to handle is difficult to achieve.

- The Drug Property

Solubility, crystal morphology, particle size and bulk density of a drug affects the final jelly characteristics.

- Mouth feel

Medicated jellies leave minimal or no residue in mouth after oral administration.

Disadvantages:

- As it is aqueous based preparation it needs appropriate packaging to maintain stability of drugs in various environment
- It may lead to unpleasant taste if not formulated appropriately.

VARIOUS COMPONENTS OF MEDICATED JELLY FORMULATION

I. Gelling Agent

These are hydrocolloids, which form gel like matrix. It dissolve in liquid phase and form weak cohesive internal structure. Examples of gelling agents:

a) Sodium Alginate

Alginate is obtained from the cell wall of brown algae .Alginates bind with water and forms thick gum. It is used in various oral and topical pharmaceutical formulations. It is generally used as thickening agent and suspending agent in various topical formulations such as pastes, creams and gels.

b) Pectin

It is a heteropolysaccharide obtained from cell walls of terrestrial plants. It is used against constipation & diarrhoea, where it increases viscosity & volume of stool. Due to its lesser cost it is used in various delivery methods like controlled release, mucoadhesive, gastroretentive, colon- specific drug delivery systems. Also used as stabilizer in cosmetics.

c) Tragacanth

Tragacanth gum works as an emulsifying and suspending agent in various pharmaceutical preparations such as emulsion, gels, and creams. Also used as thickener, stabilizer, & texturant additive in foods & pharmaceuticals.

d) Gelatin

Gelatin is generally used as gelling agent in pharmaceutical preparation, vitamin capsules, cosmetic technology, & photographic emulsions. Also used in implantable delivery system to deliver drug suspended in biodegradable matrix.

e) Xanthan Gum

It is commonly used as a thickening, emulsifying, suspending and stabilizing agents in oral, topical pharmaceutical formulations, cosmetic, and food products. Used as binder in tooth paste & keeps the product uniform. Used as a hydrocolloid in the food preparations & thickening agent in shampoos.

f) Cellulose derivatives

Used as emulsifier & thickener in food & cosmetic preparations. Also used for relief from constipation problem

E.g. Methyl cellulose, Sodium carboxy methyl cellulose.

g) Agar

Agar-agar is vegetarian product & substitute to gelatine. It is obtained from algae & is white and semitranslucent. It has various applications such as thickener, gelling agent, texturizer, moisturizer, emulsifier, flavour enhancer, and absorbent in pharmaceuticals & food products.

h) Carrageenans

It is obtained from extracts of red edible seaweeds, & are linear sulfated polysaccharides .They are mainly used as gelling, thickening, and stabilizing agents in food & pharma industry. Carrageenan is vegetarian & is used as substitute for gelatine in confectionery.

II. Sweetners

a) Sucrose

Sucrose was most preferred sweetening agent because it is soluble in water, it is economical i.e., its highest purified form can be obtained at reasonable price, physically and chemically stable in different pH. It is widely used in combination with sorbitol, glycerin and other polyols to prevent crystallization of sucrose.

Table 1: Different stages of sugar at different temperatures.

Temperature	Stages of sugar
112^{o}	Thread stage
116^{o}	Soft ball stage
120^{o}	Firm ball stage
130^{o}	Hard ball stage
143^{o}	Soft crack stage
154^{o}	Hard crack stage
170^{o}	Caramel stage

b) Dextrose

They are anhydrous & monohydrate form of dextrose, among them anhydrous form is hygroscopic in nature.

c) Mannitol

Mannitol is a white, crystalline polyol obtained by hydrogenation of fructose. It imparts a mild cooling sensation when it is chewed or dissolved in the mouth due to its negative heat of solution. It is used dusting powder

on chewing gums since does not bind water well. It is thermostable & can be used in confectionaries.

d) Saccharin:

It is an artificial sweetening agent. It is about 250-500 times sweet as sucrose. It has excellent stability, saccharin sodium & calcium has excellent water solubility.

e) Sucralose:

It is an artificial sweetener. It is thermostable and also remains stable in wide pH range. Hence it can be used in products that need a longer shelf life. Compared to sucrose onset of sweetness occurs slowly but sweetness remain for longer duration of time.

f) Sorbitol

Sorbitol is a sugar alcohol & isomer of mannitol. It is about 60% as sweet as sucrose. It is obtained from corn syrup or by reduction of glucose. It is used as humectant & thickener in cosmetics, used as laxative, formulation of soft gel capsules & in treatment of hyperkalaemia.

III. Colouring agents:

Colourants are used for the following reasons:

a) To provide aesthetic appearance to dosage forms

b) To increase patient acceptance

c) To maintain colour uniformity of the dosage form.

d) Help in product recognition and differentiation.

According to the Food drug and cosmetic Act of 1938 Colorants are classified as:

a. **FD& C colours**: These are certified colorants that can be used in foods, drugs and cosmetics.

b. **D&C colours**: It includes dyes and pigments that is used in drugs & cosmetics which are meant for ingestion & application on mucous membranes

c. **External D&C:** It includes colorants that can be used in external preparations, however its use in products meant for ingestion is not considered as safe due to their oral toxicity

Types of Colouring agents

a) **Natural Colours**

It is extracted from natural sources or chemically synthesized such as beta-carotene.

b) Mineral Colours

Example of Mineral colour include mixture of red & yellow ferric oxides gives flesh colour to calamine lotion

c) Dyes

These are synthetic chemical compounds that imparts colour when it is dissolved in a solvent such as propylene glycol and glycerine. It contains 80 to 93% pure colorant material.

d) Lakes

Lakes are aluminium salts of FD&C water soluble dyes extended on a substratum of alumina. Lakes prepared from calcium salts of FD&C dyes are also permitted.

IV. Flavouring Agents

Table 2: Flavours used as per taste taste:

Taste	Flavours used
Acidic	Orange, lemon, cherry,
Alkaline	Vanilla, chocolate, mint
Bitter	Orange, anise, lemon
Metallic	Grape, berry
Sweet	Honey, chocolate, raspberry,

V. Preservatives:

Jellies are prone to microbial attack. Preservation is must in order to avoid at all any incompatibilities between gelling agents & to retain the shelf life of product.

Eg: Methyl Paraben, Propyl Paraben, Benzoic Acid, Benzalkonium Chloride, Chlorhexidine acetate.

VI .Stabilizers

Stabilizers are used to maintain desirable properties of product .It is used to prevent the drying of jellies. Examples: Propylene glycol and Sorbitol. Chelating Agents are used to avoid any reactivity between base or medicament with heavy metals e.g. EDTA.

Table 3: Various components of oral medicated jellies

Gelling agent	Sodium alginate, pectin,
Sweetners	Sucrose, dextrose, sucralose,
Colouring agents	Natural colours, mineral
Flavouring agents	Orange, lemon, vanilla, mint
Preservatives	Methyl paraben, Propyl
Stabilizers	Propylene glycol, Sorbitol

Fig 1: Some photographs of jelly formulations.

FORMULATION OF ORAL MEDICATED JELLIES[18]

Oral medicated jellies can be prepared by using gelling agents like sodium alginate, gelatin, guargum, xanthan gum. Citric acid was used as PH modifier. Simple syrup (60%) can be used as a sweetening agent. Methyl paraben (0.18%) and propyl paraben (0.02%) can be used as preservatives. Purified water up to 100% as vehicle can be used. Accurately weighed polymer powders were dispersed in 10ml of purified water maintained at 90°C. The dispersion was stirred using a magnetic stirrer for 20min to facilitate hydration of gelling agents. Add sweetening agent with continuous stirring. Then add citric acid and preservatives with stirring. The final weight was adjusted with purified water, mixed and transferred to moulds and allowed to cool.

EVALUATION OF ORAL MEDICATED JELLIES[19]

a) Physical evaluation

The medicated jelly can be examined physically for appearance like clarity, texture, transparency, consistency.

b) Stickiness and grittiness

Texture of the medicated jelly in terms of stickiness and grittiness can be determined by mildly rubbing the jelly between fingers.

c) PH

PH of jelly can be measured using digital PH meter. 0.5 g of the weighed formulation was dispersed in 50ml of water and the PH should be noted.

d) Viscosity

Viscosity was determined using Brookefield viscometer. As the system is non- newtonian spindle no: 4 can be used.

e) Spreadability

2.5g jelly should be placed in between 2 glass slides and compressed to proper thickness by keeping 1000g weight for 5 min. The time in seconds needed to separate 2 slides were taken. Less time interval to cover the distance of 7.5cm shown better spreadability. S = W *L/T

Where S = spreadability

W = weight tied to upper slide L = length of glass slide

T = time required to separate 2 slides.

f) Syneresis

Syneresis is defined as contraction and separation of water from gel upon storage. One of the major causes for it is using lesser concentration of gelling agent. Low acylated guargum gels are mostly prone to syneresis.

g) Drug content

The jellies are selected and crushed in a mortar and then mixture equivalent to that of drug was taken and dissolved in 100ml of volumetric flask containing 6.8 PH buffer and final volume was made upto the mark. Then the solution was filtered and diluted appropriately, and analysed spectrophotometrically using uv spectrophotometer.

h) In – vitro Dissolution study

The USP paddle apparatus used for in-vitro dissolution study by using dissolution medium (900ml) was kept at 37°C +- 0.5°C and 50 rpm. 5 ml of sample should withdrawn after 10, 20, 30, 40, 50, 60, 90,120 min and sink condition is maintained by replacing fresh media. The sample were determined for drug content using UV spectrophotometer. Then % drug release was calculated after absorbance was taken.

i) Stability studies

The jelly formulations were packed in aluminium foils and stored in polyethylene containers at 0°C, 25°C/60%RH for 90 days.

Limitations of pharmaceutical jellies

- Cost-intensive production process
- Jellies requires special packaging for properly stabilization &safety of stable product. It is also shows the fragile, effervescence granules property
- Higher concentration of drug cannot be incorporated.

APPLICATIONS

- Paediatric and geriatric patients who have difficulty in swallowing or chewing solid dosage forms.
- Patients having risk of choking.
- Geriatrics who cannot swallow a daily dose of antidepressant.
- An eight-year old with allergies who desires a more convenient dosage form than antihistamine syrup.
- A patient who has no access to water for consuming dosage form.

CONCLUSION:

Pharmaceuticals jellies have aesthetic appearance and pleasant taste than any other oral drug delivery systems. It has better organoleptic properties and patient compliance. Paediatrics and dysphagia patients can utilize the formulation more effectively and easily. By controlling the viscosity of jelling agent, rate of drug release and drug plasma level can be controlled.

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