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A REVIEW ARTICLE ON ORAL JELLIES FOR PEDIATRICS

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Abstract:

Oral route is the most preferred route for better patient compliance and easy administration. Medicated oral jellies are the most attractive dosage forms for paediatrics and can be ingested without water. It is alternative to solid and liquid dosage forms. The oral medicated jellies are prepared by heating method using various kinds of polymer with different concentration. As most of the pharmaceutical drugs are bitter in taste so, taste masking is an important parameter in designing the dosage form and it is mainly done by adding sweetener and flavours. Various evaluation parameters are conducted like synergesis, viscosity, invitro drug release, drug content.

Key Words: *Oral, medicated jelly, pediatric, taste masking, gelling agent.*

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INTRODUCTION:

Oral route is the most preferred route for better patient compliance and easy administration. The administration of the drug according to the dose regimen and the dose regimen is specially made according to the patient life style. Simple dosing (one pill, once daily) can decrease adherence.

By oral route drug administration, the drug passes through the GIT, the drug is released from the dosage form in a solution at or near the optimal site for drug absorption to occur.GI fluid volume and motion can vary remarkably which has importance on drug dissolution and absorption. Additionally, transit time may also vary in various parts of the GIT depending upon the individual size and prevailing local conditions. [1]

Jelly can be defined as the soft semi solid preparation having large and small drug particles which are incorporated in it. Now-a-days, jelly candies have become very common in children as they enjoy chewing the jelly and it may use as a preferred method for drug administration as it is alternative to solid and liquid dosage form.

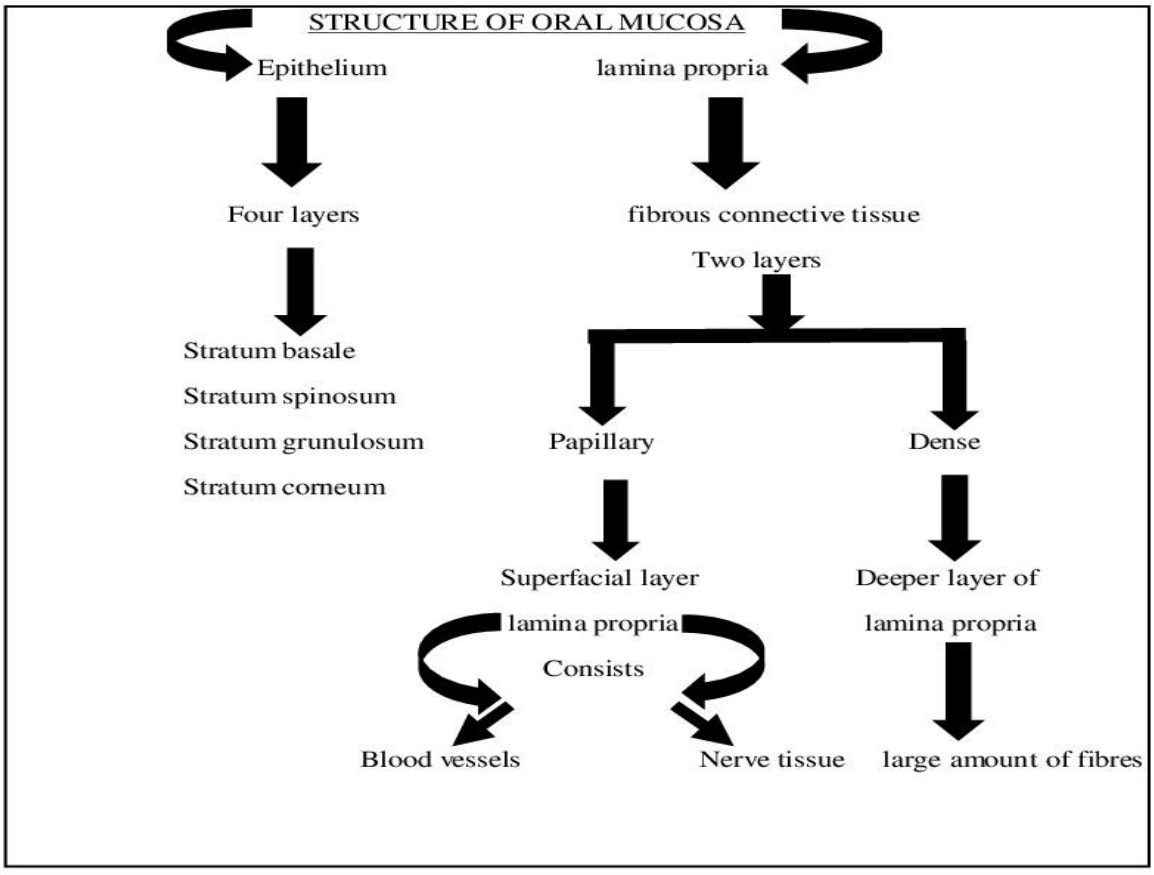
Therefore, there is scope for more patient well coming delivery system especially by oral route. In Paediatrics patient there are more compliance with ease administration and more palatable and attractive dosage forms has significantly importance in the design of novel drug delivery system. [2]

ORAL MUCOSA

It is a term used to relate the soft tissue lining of the oral cavity and it includes the –

- mucosa
- Epithelium
- Lamina propria
- Sub mucosa

The total area of the oral cavity is about 100cm^2, the oral mucosal surface is constantly washed by the saliva (daily turn is about 0.5-2L). Following structure of oral mucosa. [3]



FUNCTIONS OF ORAL MUCOSA

- ✓ Protection
- ✓ Sensation
- ✓ Secretion
- ✓ Thermal regulation
- ✓ Permeability and absorption

For all the tissue saliva act as, protective fluid and it protects from abrasion buy rough materials and from chemicals. Saliva (aqueous fluid) it mainly contains 1% organic and inorganic materials. The major framework is the flow rate which mainly depends upon the type of stimulus and degree of stimulation. The salivary pH ranges from 5.6 to 7.9 it depends upon the flow rate. [4]

THREE TYPES OF ORAL MUCOSA

1. Lining mucosa
2. Masticatory mucosa
3. Specialized mucosa

It is broadly divided into keratinized and non-keratinized.

- Keratinized oral mucosa – masticatory mucosa
  Oral and outer epithelium

- Non-keratinized oral mucosa – lining mucosa
  Specialized mucosa

Although, in the oral mucosa the mucus is released by the salivary glands.70% mucin is found in the saliva. For mucoadhesion the mucus criss-cross carries a negative charge at physiological ph. At this pH, mucus forms a strong cohesive gel structure that attach to epithelial cell surface as a gelatinous layer. [3]

GASTROINTESTINAL TRACT

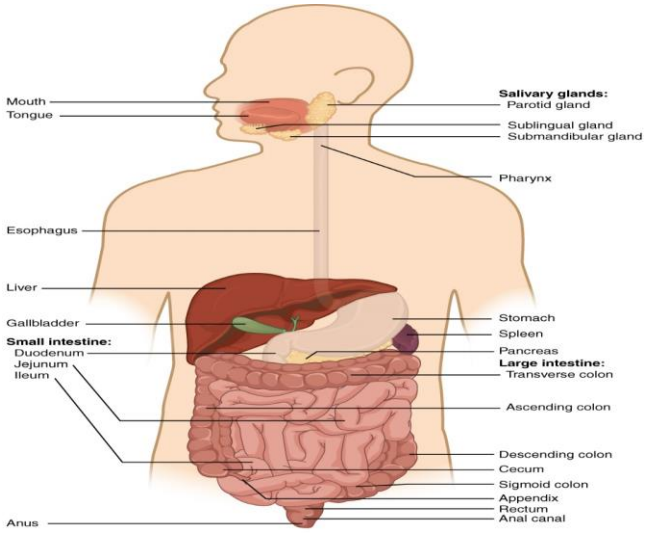
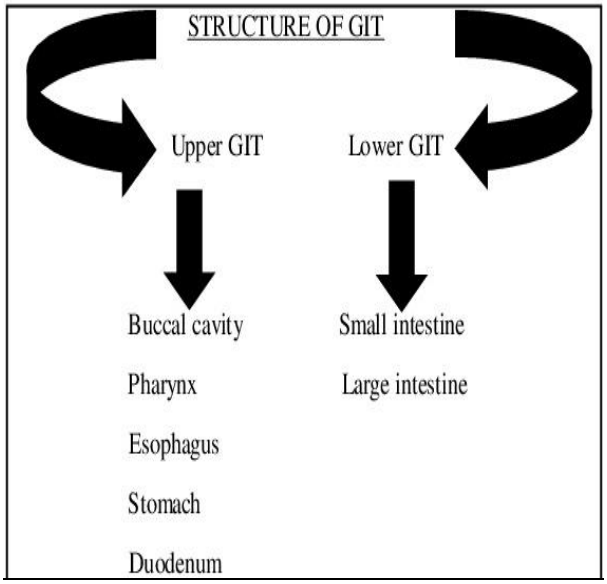


Fig.1: Gastrointestinal tract [5]

It includes from the mouth to anus and it is divided into two parts:

1. Upper GIT
2. Lower GIT

It's about 9mtr(30feet) it releases various hormones to regulate the digestive process.



THE GI DIVIDED INTO FOUR LAYERS:

1. Mucosa
2. Submucosa
3. Muscular layer
4. Serosa and adventitia

FUNCTIONS OF GIT:

1. Digestion
2. Absorption
3. Excretion
4. Protection

The pH of upper portion is 4-6.5 and lower portion pH is 1.5-4.

TASTE MASKING

In oral administration the taste is the important parameter, the desirable taste is the better choice for paediatrics it is one of the pharmaceutical parameter. Taste buds plays the role of taste and they are around 10,000. The chemoreceptors pass signals to brain for the perception of taste. As most of the pharmaceutical drugs are bitter in taste so, taste masking is an important parameter in designing the dosage form and it is mainly done by adding sweetener and flavours.

TYPES OF TASTE

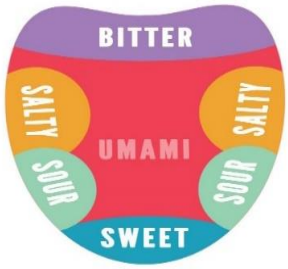


Fig.2: Diverse types of taste on tongue. [6]

1. Sweet
2. Salty
3. Sour
4. Bitter
5. umami

STRUCTURE

TONGUE – It is a muscular structure and its inside the mouth reddish pink colour having V-shape and grooves.

Function –

1. Help in taste
2. Help in Speech
3. Help in chewing and swallowing food

Parts of tongue -

1. Papillae
2. Sulcus terminalis
3. Tonsils
4. Adenoids
5. Frenulum lingue

TASTE BUDS

The taste buds are the small pores on the surface of tongue known as papillae

It's of three types:

1. Fungiform papillae
2. Foliate papillae
3. Circumvallate papillae

Its structure is like onion having group of receptor cells (50-100 cells) it gives perception of taste by sensory neurons to CNS. As there are four types of taste on tongue at different regions like sweet on top of the tongue, sour at sides, salty on edges and upper portion and bitter on back of the tongue. [7]

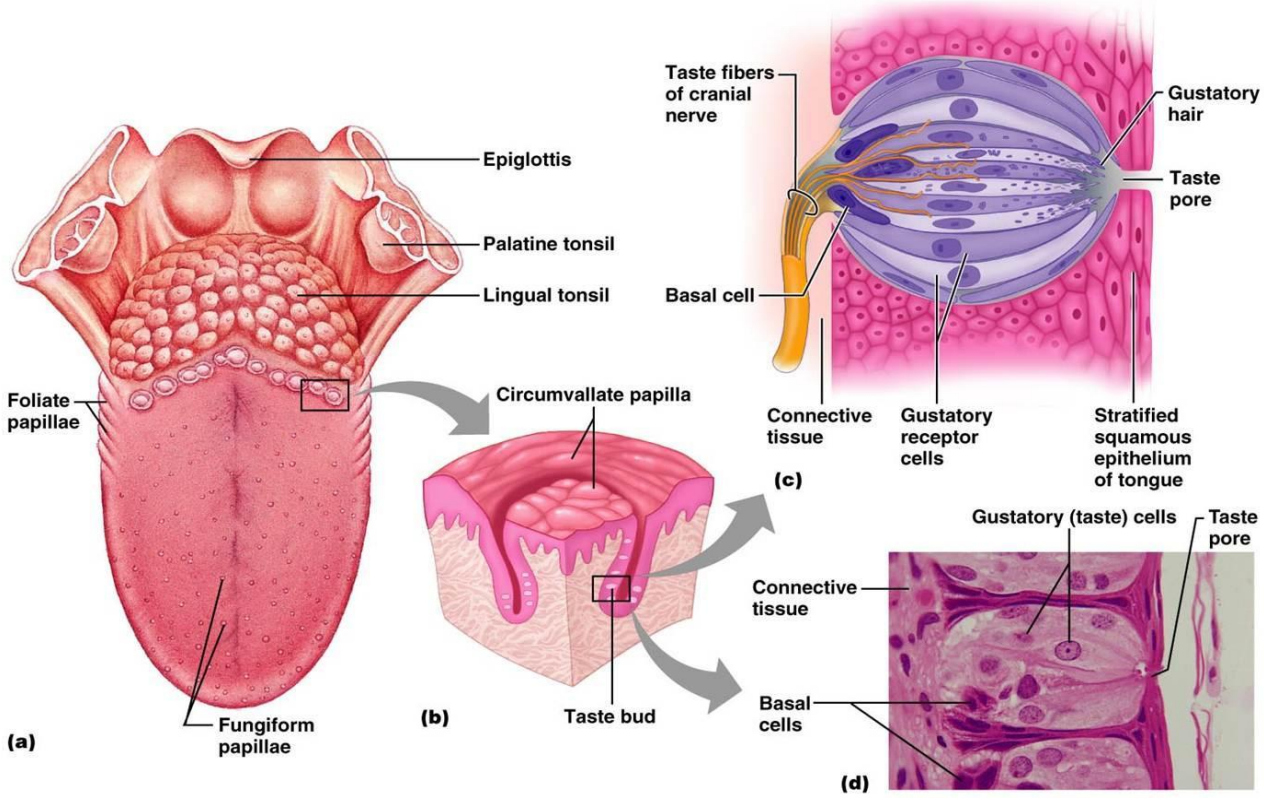


Fig.3: Activity of taste buds. [8]

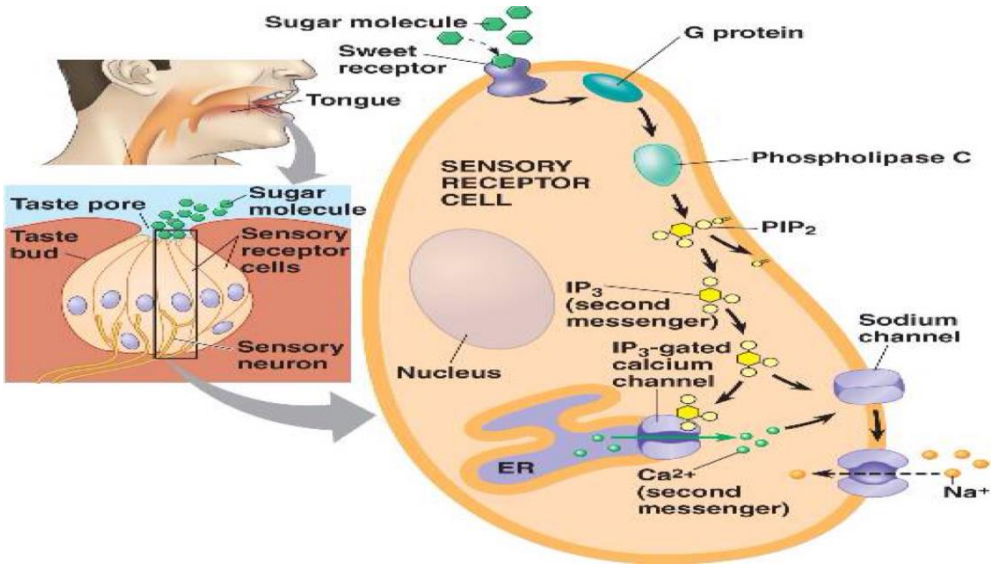


Fig.4: Mechanism of action. [10]

MECHANISM OF ACTION

The sensation of taste is imparted by taste bud as these are the chemoreceptor triggered by the chemicals(drug) which are dissolved in saliva and it binds with the G-protein coupled receptor and it release G-protein called as gustducin. It activates effector enzyme phosphodiesterase IA or phosphodipase C beta2 and it changes intracellular level of second messenger such as cyclic adenosine monophosphate, inositol,1,4,5-triphophate and diacylglycerol then it activates ion channel and the depolarization occurs. The release of neurotransmitters which sends the nerve impulse into the brain and produce a sensation of taste. [9]

INTERACTION BETWEEN TASTE AND COMPOUND ACCORDING TO CHEMICAL STRUCTURE

There is an interconnection between chemical structure and taste. The degree of ionization, solubility and various kind of ions produced in the saliva certainly master the perception interpreted by the brain. Sweet taste is due to polyhydroxy compounds, polyhalogenated aliphatic compounds and amino acid. The positive effect is balanced by the nearness of a negative group, amino and amide it may produce sweet taste. With increased number of hydroxyl group the solubility is increased so by that sweetness also increases. Sour taste is originated by hydrogen ions and it is directly proportional to lipid solubility and the hydrogen ion conc. of the compound. Salt taste is concurrent existence of anion and cation for example: ammonium chloride, potassium bromide and sodium salicylate. These are the features of acids, alum, lactones, tannins and phenols. Bitter taste is produced by the high molecular weight salts or compounds like free bases i.e, alkaloids and amides. [11]

The substance with minimum concentration that elicit sensation of taste. The below table shows the threshold concentration of four tastes: [12]

TASTE	THRESHOLD CONC.
Sweet	0.007%
Sour	0.25%
Salt	0.00005%
Bitter	0.5%

APPROACHES USED TO REDUCE BITTER TASTE OF DRUG

1. Decreasing the drug solubility at the pH 56 to 6.8 of saliva.
2. Drugs which involves with the taste receptor its nature and affinity can be changed.

TASTE MASKING IS AFFECTED BY NUMEROUS FACTORS

1. Dose of active pharmaceuticals
2. Particle size and distribution of drug
3. Solubility of drug
4. Dosage forms
5. Drug ionic characteristics

TECHNIQUES OF TASTE MASKING

Various techniques are there for masking the taste to give pleasant taste. They are as follows:

1. Flavours and sweeteners
2. Prodrug
3. Incusion complexes

4. Coating polymer and drug particle
5. By granulation
6. Ion exchange resin
7. Microencapsulation
8. Multiple emulsion technique
9. Gelation technique
10. Viscosity modifification
11. Hot melt extrusion
12. pH modifiers
13. Miscellaneous. [13]

ORAL MEDICATED JELLY

Oral medicated jellies are unit dosage form, these formulation offers rapid dissolution and absorption of drug through oral mucosa therefore show early onset of action. Most of the pharmaceutical ingredients are bitter in taste so the taste masking is done by using sweetener i.e. sugar and various flavours. In this oral medicated formulation, the jelly is chewed without ingestion of water and the active ingredients i.e., drug will be released and mixed with saliva and then swallowed and introduced into the GI.

As the jelly remain solid during storage for stability and it transformed into highly viscous liquid after its administration. Jellies are formed by intensification of polymers like gelatine, guar gum, gellan gum, pectin are widely used. By choosing the right gelling agent at suitable concentration, the drug released slowly from the jelly vehicle. The main aim is to develop the hydrophilic jelly dosage form for oral administration. [14]

The medicated jelly is mainly used for oral diseases as well as systemic diseases. It is useful for the pediatric patients because it's like candy and they can easily take this medication as having attractive colour and sweet taste and they love chewing the jelly having different shapes and size.

Pediatric population include the neonates, children(2-11yrs), adolescents (12-16/18 years).

TYPES OF ORAL JELLY

There are three types of jellies:

Medicated jelly: These are chiefly used on mucous membrane and skin for their spermicidal, local anaesthetics, and antiseptic properties. These jellies contain sufficient water. After evaporation of water, jellies provide a local cooling effect and residual film gives protection. For example, ephedrine sulphate jelly is used as a vasoconstrictor to arrest the bleeding of nose.

Lubricating jelly: These jellies are used for lubrication of diagnostic equipment such as surgical gloves, cystoscopes, catheters

Miscellaneous jelly: These are meant for various applications like patch testing, electrocardiography etc. [15]

ADVANTAGE OF JELLY

1. Patient convienent and ease administered.
2. Patient acceptability.
3. More palatable the formulation, the higher the dose volume can be tolerated.
4. Choking hazard is decreased.
5. Ingested without water.

DISADVANTAGE OF JELLY

1. There is stability and degradation problem.
2. Problem of dose measurement.
3. Interpatient variability around the age of 6 yrs. [16]

EXCEPIENTS USED IN ORAL JELLY

A)	GELLING AGENT:	Pectin Tragacanth Gelatine Xantham gum Gellan gum Carrageenans Guar gum Sodium alginate Cellulose derivative
B)	STABILIZERS:	Propylene glycol Sorbitol
C)	PRESERVATIVE:	Methyl paraben Propyl paraben Benzalkonium chloride Sodium benzoate
D)	SOLUBILIZERS:	Cremophore RH40 PEG 400
E)	pH MODIFERS:	Citric acid
F)	SWEETNERS:	Simple syrup Acesulfame potassium
G)	FLAVOURS:	Strawberry Vanilla Orange

LIST OF SOME DRUGS USED IN ORAL JELLY

A)	ANALGESICS:	Ibuprofen Paracetamol Diclofenac
B)	ANTI-HELMINT:	Albendazole Mebendazole
C)	ANTI-EMETICS:	Domperidone Ondansetron
D)	ANTI-HISTAMINES:	Citrizine Cinnarizine
E)	LEUKOTRIENE ANTAGONIST:	Zafirlukast Montelukast
F)	ANTI-DIABETIC:	Metformin Glibenclamide

METHOD OF PREPARATION

1. The jellies were prepared by using different polymers of different quantities

2. The sugar syrup will be prepared.
3. To the sugar syrup the gelling agent is added with continuous stirring and heated.
4. As the gelling agent dissolves completely, stabilizers and solubilizes are added to it and boiled for few minutes, thoroughly mixed.
5. When the mixture was completely dissolved, preservatives are added to it with continuous stirring.
6. Then, drug was added to it with continuous stirring, colour and flavour was added, jellies could have settled down and thoroughly mixed.
7. The final weight was adjusted with purified water.
8. Then, transferred into moulds and the mixture could cool to room temperature to form jelly.

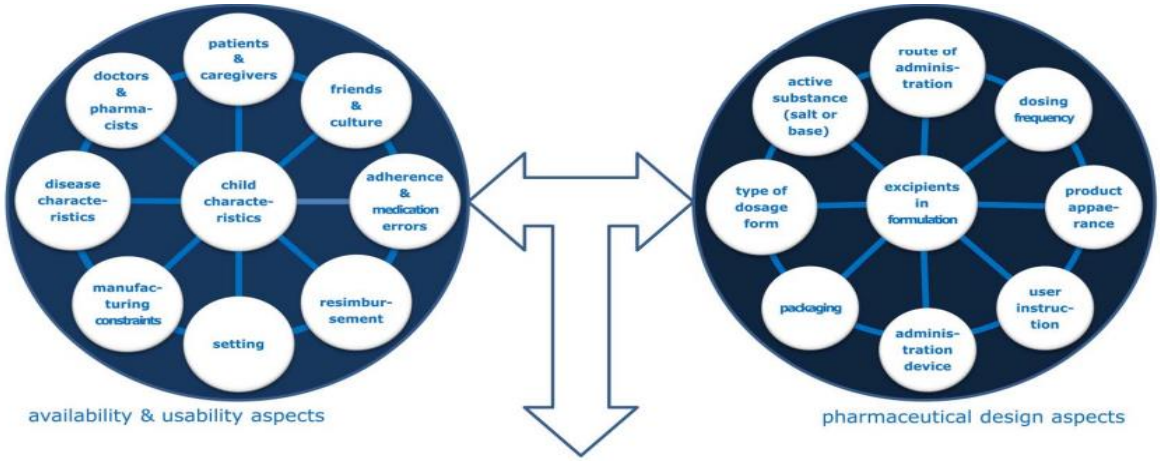
EVALUATION PARAMETERS FOR ORAL JELLY

1) PHYSICAL APPEARANCE – The oral jelly was subject for clarity, odour, consistency and texture
2) WEIGHT VARIATION – it is determined by the average weight of ten jellies as they are taken out of moulds in a beaker and individually weighed and mixed.
3) STICKINESS AND GRITTINESS- It is determined by rubbing the jelly between two fingers the stickiness and grittiness is checked visually.
4) POURABILITY OF THE MIXTURE- The main property of jelly is that it can easily pourable into the moulds by addition of buffer salt which act as a retardant for example trisodium citrate these retardants generally increases the pH the formulation earlier the addition of acid hence halts pre-gelation. As the concentration is high of retarder, the lower the setting temperature and longer the setting time this helps in setting and pouring of the jelly
5) pH DETERMINATION – The pH is determined by digital Ph meter as jelly is dispersed in distilled water (50%) and 1%solution is prepared, the pH was noted.
6) CONTENT UNIFORMITY – This evaluation is performed for every dosage form to assure the equality of content in drug substance. It is done by crushing and then mixing the jelly, the extraction of this mixture is done by using suitable media and the amount of drug was determined by analytical method.
7) VISCOSITY – Viscosity is measured by Brookfield viscometer and by using fresh sample every time.it is calculated by:
   Viscosity in centipoise = Dial reading × factor [2]
8) SPREADABILITY – Spreadability is measured by applying the jelly in between of two glass slides and flatten to unvarying extent by putting weight of 1000gm. The time taken by the two slides to separate was estimated to spreadability.it is calculated by:

a. $S = m \times L/T$
b. Where m = weight tide to upper slide
c. T = time taken
d. L = length moved on glass slide

9) STABILITY STUDIES – Stability studies are determined according to ICH guidelines and can be evaluated by carrying out the prepared jelly i.e, stored for 90 days at room temperature and analysed like the change in physical appearance.
10) SYNERESIS – It is a separation of liquid by the contraction of gel and the jelly preparation was evaluated after 24hour at room temperature.
11) MICROBIAL STUDIES – These studies are important parameter for determining the microbial profile of jellies. as jellies are more prone to microbial growth due to presence of water. The jellies were tested for culturing pathogens on specific medium for E. coli, S.aureus and P.aeruginosa.
12) PERCENT DRUG CONTENT – Consistent gel was prepared by compressing 20 jellies. specified quantity of gel equivalent to 50mg of drug and to this sufficient water is added, mixed completely. Sonicate the solution for 45 min and then make up the volume upto 50ml, filter and dilution were prepared. Thus, the absorbance is checked by using UV spectroscopy.
13) INVITRO TASTE ANALYSIS – 5ml simulated salivary pH was used to analyse the taste competency of prepared jelly. One jelly from each batch placed in 5ml solution in a 50ml beaker for 60sec to 120sec, solution is the filtered respectively. By using UV, filterates were examined for drug content.
14) DISSOLUTION STUDIES - USP type 2 paddle apparatus was used to perform invitro dissolution study at 50rpm. For dissolution medium 900ml media was used at temperature 37˚C±0.5. [17]

ASPECTS FOR PEDIATRIC FORMULATION



SAFE AND EFFECTIVE FORMULATION

Key aspects involve the development of (novel) dosage forms such as jelly formulations, the safety of excipients, child acceptability and the importance of suitable dosing devices. The acquired knowledge is useful to formulation scientists as well as to doctors, pharmacists and caregivers when prescribing, compounding, dispensing or administering medicines to children.

CONCLUSION:

There are several methods adopted and utilised for the taste masking of bitter drugs. In respect to pediatric age group medicated jellies has the potential to evolve as one of the most popular dosage form. Its unique properties help us to improve better patient compliant in respect to pediatric group. It also able to provide prominent therapeutic effectiveness by early onset of action as having quick absorption and dissolution of drug. Oral jellies are alternative to solid dosage form as they possess both liquid and solid property and its having ease administration without ingestion of water. Therefore, the oral medicated jellies are an accepted technology.

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