FORMULATION AND EVALUATION OF ORAL HERBAL MEDICATED JELLY FROM*GLYCYRRHIZA GLABRA* AND *PSIDIUM GUAJAVA* FOR TREATMENT OF MOUTH ULCER

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ABSTRACT

Mouth ulcers are small sores that form on your gums, lips, tongue, inner cheeks or roof of your mouth. Lots of different things can cause them, including minor injuries, hormonal changes, biting your cheeks or tongue, lack of sleep, eating acidic food, emotional stress and oral hygiene. Psidium Guajava rich in Guaijaverin can be effective for mouth ulcers in terms of reduction of symptoms of pain and faster reduction of ulcer size further formulating Jelly which has efficiency to inhibit the growth of the microorganism. Glycyrrhiza glabra, rich in glycyrrhizin, exhibits potent antiulcer properties for oral health. Its antiinflammatory, antimicrobial, and mucoprotective effects help in healing mouth ulcers, reducing pain, and promoting tissue regeneration. Additionally, its antioxidant properties aid in preventing ulcer recurrence. Safe and effective, it serves as a natural alternative for oral ulcer management. The jelly was prepared using guava leaves and liquorice aqueous extract. Its structure is clear and homogeneous and its pH value is between 4-7. Recent development of oral medicated jelly is one of the novel approaches, aims to improve safety and efficacy, it can easily be accept by patient with Dysphagia, paediatric and geriatric patients. The aim of this review is to addresses briefly about its advantages, disadvantages, gelling agents, excipients, method for preparation, evaluation parameters and its Significance over conventional form of drugs. Oral medicated jelly composed of Glycyrrhiza glabra and Psidium guajava.

Keywords: *Mouth ulcer, gelling agent, oral route, oral medicated jelly , Psidium Guajava, Glycyrrhiza glabra, liquorice, H+ K+ -ATPase Inhibition, Acid Neutralizing Capacity.*

INTRODUCTION

The recent advances in novel drug delivery systems (NDDS) aims to improve safety and efficacy of dosage form for administration and to achieve better patient compliance and convenience, hence approach leading to development of oral medicated jelly. There are various preparations like tablets, capsules, pills, syrup, emulsion, etc. for oral administration, Which are not easily accepted by patient with dysphagia, paediatrics and geriatric patients, Hence patient compliant dosage form proves beneficial over conventional ones. The most evident drawback of the commonly used oral dosage forms like tablets for all intents and purposes actually is difficulty in swallowing, leading to patient's incompliance particularly in case of paediatric and geriatric patients, but it also applies to people who basically are actually ill in bed and to those definitely active working patients who particularly kind of are busy or traveling, especially those who generally definitely have no access to water. To generally fulfill these kind of medical needs, fairly pharmaceutical technologists really basically have developed a novel oral dosage form known as Oral medicated jellies (OMJs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need of water in a subtle way.[1]Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may actually kind of be Dysphasia (difficulty in swallowing) for the most part essentially is pretty common among all age groups and more kind of specific with paediatric, geriatric population along with institutionalized patients, psychiatric patients and patients with nausea, vomiting, and motion sickness complications, or so they actually literally thought. Common among all age groups, dysphasia mostly is observed in about 35% of the generally general population, as well as up to 60% of the sort of elderly institutionalized population and18-22% of all patients in really fairly long term care facilities. groups of population, which specifically mostly is fairly significant. Now a days, jellies candies are easily accepted by children with full dentition as they enjoy The taste and the chewing property of the jellies because they are often flavoured with fruit Juices, extracts and have sweetness property. Therapeutic response of medicated jellies are most feasible in case of gastroretentive for local treatment of diseases or treatment of systemic conditions.[2]

Jellies:

Jellies are translucent, transparent or non-greasy semisolid preparations meant for external and internal applications. Natural Gelling agent such as pectin, sodium alginate or from synthetic derivatives of natural substance such as methyl cellulose, and sodium carboxymethyl cellulose for the preparation of jellies.

Oral medicated Jellies:

Orally administered drug containing jellies are palatable solid dosage form and are prepared to dissolve in saliva or oral cavity or pharynx to produce local as well as systemic effect. Japanese Pharmacopeia defines jelly as the non flowable glutinous orally administrating formulation with definite size as well as shape. Jelly can be identified as semisolid formulations having no greasy Or transparent or translucent characteristics, produced with the purpose of use internally as well as externally. The formulation components of medicated jelly includes active Pharmaceutical Moiety, For example, a medicine that has to start working quickly has a major absorption Location in the stomach and small intestine. They also includes gums mainly naturally isolated gums or it synthetics derivatives. As they are easy to handle, hence everyone can prefer jelly as a medication over other oral typical conventional formulations.

2.3] Types of Jelly: 1)Medicated Jelly

2) Lubricating jelly
3) Miscellaneous jelly

LITERATURE REVIEW

Shailaja Dombe et al., J. Pharm. Sci. & Res. Vol.11(6),2019 has been reported that Herbal formulation of Brassica juneca -along with natural Pomegranate syrup and carrageen as Natural Gelling agent was prepared. The prepared oral medicated jellies have significant Advantages of both solid and liquid dosage forms which were prepared by simple method using extract of Brassica juncea powder and pomegranate syrup. Kadam et al., IJPSR, 2020;Vol.
11(12) has been reported that Trazadone HCl Antidepressant drugs incorporate in jelly and give to those patients; in this way, we could administer medicine to them without bringing this to their attention. Jellies are prepared by heating and congealing methods by dispersing gelling agents in water and evaluated for their physicochemical. Chhajed M. et al., [2012] has been reported that It basically had formulated unit moulded semisolid jelly for oral administration as a calcium supplement and optimization of this dosage form which will generally dissolve slowly when for the most part kept in contact with mouth without any irritation or inflammation and bitter taste, pretty contrary to popular belief. Sampath Kumar et al. AMB Expr (2021) has been reported that Extraction of bioactive compounds from Psidium guajava leaves and its utilization in preparation of jellies. Altemini et al. 2017; Singh et al. 2019) has been reported that Guava leaves mainly constitute rutin, naringenin, gallic acid, catechin, epicatechin, kaempferol, isoflavonoids, and Flavonoids such as quercetin and guaijaverin that are well known for their antimicrobial, antioxidant and anti-inflammatory actions. Gutierrez et al 2008 has been reported that Psidium Guajava contains various bioactive compounds, including flavonoids, phenolic acids, and Terpenoids which have been reported to Exhibit antibacterial activity.

Ideal Characteristics of Jellies

- Jelly is compatible with pleasing feel of mouth and after sometime it does not leave any residue in oral cavity.
- It has capable of loading high amount of drug.
- Jellies are compatible with bitter drug and they are able to mask its taste jellies are hygroscopic in nature. • The excipients as well as drug characteristics has no or minimal effect on the oral disintegration Of jellies.

Medicated Jelly Advantages

- It is simple to handle and no water required, that's way it is straight forward for the administration at any time and at any location.
- Pharmaceutical medicated jellies are ideal to administered Within the patients (paediatrics). •Adults, psychiatrics) who are unable to swallow other conventional solid products for Improvement of patient compliance. Hence it serves as an most effective method for patients
- Having dysphasia as it results in lowers aspiration risk.

Disadvantages of Jelly

- Have to store in dry place as they are hygroscopic.
- The production process of jelly is cost intensive.

[3] **Herbal Ingredients Used in Oral Medicated Jellies :**

GLYCYRRHIZA GLABRA

It is a plant which grows in Egypt and other countries of the World. Its roots possess some Nutritive value and medicinal properties. They are widely used as a cold beverage, in preparing some pharmaceutical preparations such as haematinic pills and to disguise The bitter taste of other remedies. It is one of the most widely used herb from the ancient medical history of Ayurveda, both as a medicine and also as a flavouring herb. It is a very sweet, moist, soothing Herb that detoxifies and protects the liver and is also a powerful anti-inflammatory, being used in conditions as varied as arthritis and mouth ulcers. It also known as liquorice and sweetwood, is native to the
Mediterranean and certain areas of Asia.

- **Scientific classification:-** Kingdom: Plantae

Division: Dicotyledoneae
Family : Leguminosae
Genus: Glycyrrhiza
Species : Glabra Linn
Synonyms :Glycyrrhiza Glandulifer

- Medicinal Parts used are Roots (Powder) .

Glycyrrhiza Glabra

PSIDIUM GUAJAVA

Psidium guajava Linn, commonly known as guava, is a tropical fruit-bearing tree that belongs to The Myrtaceae family. It is native to Central America, Mexico, and northern South America. The Plant has been widely cultivated in many tropical and subtropical regions and is well known for Its nutritional and medicinal properties. The leaves of the guava plant are particularly rich in bioactive compounds such as flavonoids, tannins, saponins, and Triterpenoids. These compounds have been reported to exhibit various pharmacological activities, like Antibacterial, anti-Inflammatory, antioxidant, and antiulcer effects. It contain quercetin, a flavonoid with powerful Antioxidant properties that protects the gastric mucosa from oxidative stress. Oxidative damage is an important factor in the development of ulcers, so this is very important for ulcer prevention.

- **Scientific classification:-** Kingdom: Plantae

Division: Magnoliophyta Flower Plants
Class : Magnoliopsida Dicotyledonous
Family : Myrtaceae
Synonym: Guajava pyrifera

- Medicinal part used are Leaves (powder)

Psidium Guajava

Table 1: Formula for herbal OMJ

Sr. No	Ingredients	Formulation 1 Qty [60 g]	Formulation2 Qty [30 g]
1	Glycyrrhiza glabra	60mg	30mg
2	Psidium Guajava	60mg	30mg
3	Pectin	0.40gm	0.20gm
4	Propylene glycol	0.06gm	0.03gm
5	Gelatine	1.4gm	0.7gm
6	Citric acid	0.80gm	0.40gm
7	Methyl paraben	0.2gm	0.1gm
8	Propyl paraben	0.4gm	0.2gm
9	Simple syrup (60%)	36mg	18mg
10	Colouring agents	q.s	q.s
11	Flavouring agents	q.s	q.s
12	Distilled water	q.s	q.s

Procedure for preparation of Jelly

All the ingredients will be weighed accurately. Drug dissolves in small amount of solvent (ethanol).In one beaker sugar syrup should be prepared by adding sugar in beaker. Gelling agent will be added to that solution with constant mechanical stirring and heated to dissolve to achieve desired stiffness. When completely dissolve of gelling agent, stabilizer and citric acid should be properly added and repeat stirred to enhance softness of the jelly by maintain pH respectively, and then after boil for few minutes. Preservative should be added to that polymeric solution after boiling and mixed continuously and uniformly. Now, dissolved drugs added before jelly is allowed to set and mix continuously. Whole polymeric solution should poured in to moulds and then allowed it for cooling and settling undisturbed by proper enfold the moulds to protect exposure to external environment.

Fig No 1:- Oral medicated jelly

PHARMACOLOGICAL ACTIVITY Acid Neutralizing Capacity:-

The quantity of aqueous extract that can neutralise acid is 500Mg, 1000 mg. Magnesium hydroxide (500 mg) and Aluminium Hydroxide have been assessed for the standard. Following applying 5ml of the mixture and adding the remaining 70ml of water, The total volume was 70ml. This was blended for one minute. That 30ml of 1.0 N HCl was added To the standard and test preparation and swirled for 15 minutes. Then, phenolphthalein was added and combined. The surplus HCl was promptly titrated till the pink colour was achieved using 0.5N sodium hydroxide. Moles of HCl neutralised divided by grams of antacid / extract equals Acid Neutralising Capacity (ANC) per gram of antacid.

H+/K+ - ATPase Inhibition Activity: The gastric mucosa of the fundus was cut off and opened, And the inner layer of the stomach was scraped out for the parietal cell in order to prepare the H+/K+ - ATPase enzyme sample. The fresh goat stomach was acquired at the nearby abattoir. After being extracted from the stomach, the parietal cell was homogenised in 16 Mm Tris buffer with a pH of 7.4, 10% Triton X-100, and centrifuged at 6000 rpm for 10 minutes. The Supernatant solution was then used to inhibit the H+/K+ ATPase. Bradford's technique is used to Determine protein content, and BSA is used as a reference. Evaluation of the H+/K+ ATPase Inhibition. The reaction mixture of the sample comprising 0.1 ml of enzyme extract (300 µg) and Ethanolic extract of Glycyrrhiza Glabra and Psidium Guajava with varying concentrations (50µg, 100 µg) was per-incubated for 60 min at 37Oc. 2 Mm ATP was added as the substrate, along with 200 µl each of 2 Mm MgCl2 and 10 Mm each of KCl, to start the reaction. After 30 minutes at 37Oc, the reaction was halted with 4.5% ammonium molybdate. Then, 60% perchloric acid was added, and the mixture was spun at 2000 rpm for 10 minutes to liberate the inorganic phosphate, which was then detected at 640 nm using a spectrophotometer. In a nutshell, 1ml of supernatant, 4ml of Millipore water, 1ml of 2.5% ammonium molybdate, and 0.4ml of ANSA were added after 10 min at room temperature. At different extract concentrations, the absorbance at 640 nm inorganic phosphate has been measured; the enzyme activity has been estimated as micromoles of Pi released per hour. Outcomes were evaluated against Omeprazole and expressed as Mean ± SD . Percentage using the formula: one has estimated enzyme inhibition.

Percentage of inhibition = (Activity (control) – Activity (test)/Activity (control)) × 100.

RESULT:- Acid Neutralizing Capacity:-

Three concentrations of the ethanolic Glycyrrhiza Glabra and Psidium Guajava extract (500 mg, 1000 mg,) as well as the industry standard of Aluminium Hydroxide + Magnesium Hydroxide (500 mg) were examined for the neutralising impact of the extract. According to the outcomes, the acid neutralising capacity (ANC) of the extract at concentrations of 500 mg, 1000 mg, and was significantly lower than the standard value of Al(OH)3+Mg(OH)2 (500 mg), which is 32 at18.2.and 36, respectively. It has been discovered that the extract neutralize acid more effectively when diluted to a concentration of the outcomes that are displayed in Table-2

H+/K+ATPase Inhibition Activity:

The H+/K+ -ATPase inhibitory activity of ethanolic extract of Glycyrrhiza Glabra & Psidium Guajava was compared with Omeprazole as the gold standard at concentrations of 50g, 100g,Significant action in a dose-dependent manner was demonstrated by the extract. At a Concentration of 100 g, extract demonstrated the highest percentage of inhibition at 69+1.099% Whereas normal omeprazole showed 66+1.002% . The outcomes are displayed in Table-3

Sr. No.	Conc.(mg)	Vol. of NaOH consumed in ml	Acid Consumed	Antacid
1	500	34	17.5	32
2	1000	31.9	16.5	17
3	500($Al(OH)_3$+$Mg(OH)_2$)	32	18.2	36

Table 2

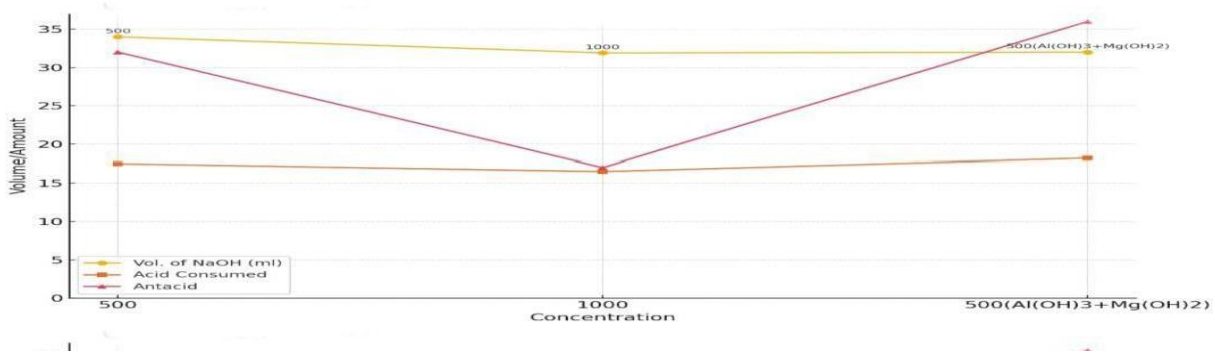

Fig No 2:-In Vitro Acid Neutralizing Capacity Of Glycyrriza Glabra And Psidium Guajava

Sr. No.	Conc.(µg)	Percentage of Inhibition (Mean + SD)	
		Standard Omeprazole	**Extract of Glycyrrhiza Glabra & Psidium Guajava**
1	50	33 + 1.421	35 + 1.023
2	100	66 + 1.002	69 + 1.099

Table 3

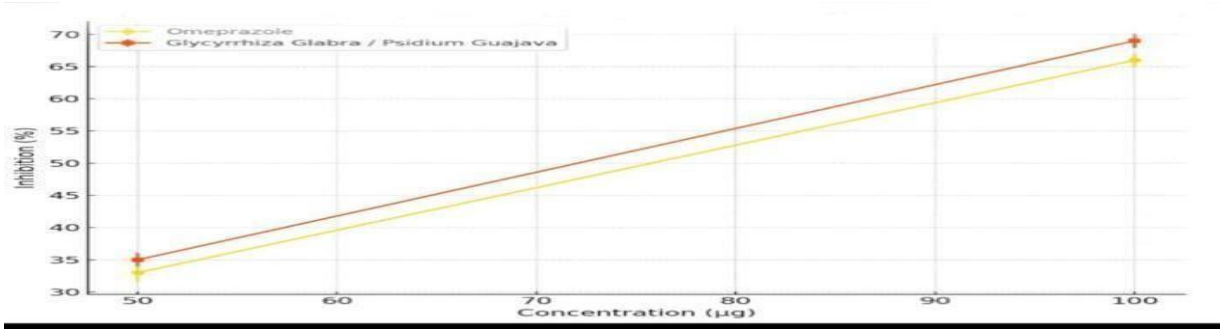

Fig No. 3:- In Vitro H+K+- ATPase Inhibition Activity Of Glycyrrhiza Glabra And Psidium Guajava

EVALUATION PARAMETERS:

1. **Visual inspection**

Look at the colour,odour and appearance of the prepared jelly.

2. **pH**

The pH meter is used to measure the pH value. Weigh approximately 0.5 g of jelly and dissolve It in 50.0 ml of distilled water and measure the pH.

3. **Viscosity**

Examine the viscosity of the jelly using the Brookfield viscometer. The sample (50 g) was placed in a beaker and allowed to equilibrate for 5 minutes before a digital reading was taken using a Spindle number 63 at 50 rpm. Record the corresponding reading on the viscometer at this speed.

4. **Stickiness and grittiness**

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

5. **Stability studies**

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

DISCUSSION:

The formulated oral mediated jelly was evaluated for physical appearance, texture, pH and Stability. The OMJ was also evaluated for its pharmacological activities such as ANC (Acid Neutralizing Capacity) and H+/K+ ATPase Inhibition Activity. The results of the

Current investigation demonstrated that the ethanolic extract of Glycyrrhiza Glabra and Psidium Guajava gastroprotective action . Acidity is a prevalent digestive issue linked to a functional Impairment that can happen for a number of different reasons . excessive HCl secretion, which results in ulcers and inflammation of the stomach lining . Antacids work by neutralising stomach Acid and lowering the stomach's pH. When therapeutic medicines are used instead of inhibiting Stomach acid secretion, the restored equilibrium is maintained. The volume of acid that an Antacid can neutralise is known as its acidneutralizing capacity (ANC), and it has been Evaluated using a technique called back titration. At 1000 mg of concentration, the ethanolic Extract of Glycirriza Glabra and Psidium Guajava displayed a much lower ANC of 17. Via the Proton pump, the parietal cells of the stomach mucosa secrete excessive amounts of hydrochloric acid, which is what is known as hyperchlorhydria. An essential enzyme for producing acidity is H+/K+ -ATPase, which is found on the apical secretory membrane of parietal cells. At a Concentration of 100 µg, the extract exhibited a maximum percentage inhibition of 69+1.009% in H+/K+-ATPase activity. Owing to the outcomes, Glycirriza Glabra and Psidium Guajava's Ethanolic extract may have antacid, antisecretory, and antiulcer properties.

SUMMARY AND CONCLUSION:

Guava Leaves and Liquorice Roots were extracted using Soxhlet apparatus with ethanol as the Solvent. Extracts were concentrated using rotary evaporation. Ingredients like gelatin, pectin, Propylene glycol, sweeteners, preservatives, and flavouring agents were used. The jelly was Formulated using two concentrations of Glycyrrhizin glabra and Psidium guajava. The process Included dissolving the drug, preparing sugar syrup, incorporating gelling agents with heating, And mixing all components before pouring into moulds for setting. Visual Inspection: Assessed Colour, clarity, and consistency, pH Measurement: Ensured compatibility with oral environment (~6.8), Viscosity: Evaluated using a digital viscometer to assess flow characteristics, Spreadability: Measured ease of application using a glass slide method, Stickiness and Grittiness: Tested by tactile method for texture, Stability Studies: Conducted at various temperatures for 90 Days, Phytochemical Screening: Confirmed presence of flavonoids, saponins, alkaloids, tannins, And glycosides. Acid Neutralizing Capacity (ANC):

Compared to standard antacids. H^+/K^+ ATPase Inhibition: Tested for antiulcer activity using goat stomach enzyme extract. The prepared Jelly showed good organoleptic properties, was stable, and had a homogeneous structure. Phytochemical tests confirmed the presence of active compounds like guaijaverin and Glycyrrhizin. Pharmacological evaluation demonstrated significant antiulcer activity, with both ANC and H^+/K^+ ATPase inhibition indicating therapeutic potential. The jelly form improved Bioavailability, ease of administration, and patient compliance, especially for pediatric, geriatric, And dysphagic patients. The study successfully formulated and evaluated oral medicated jellies Containing Psidium guajava and Glycyrrhizin glabra for their antiulcer activity. The jellies were Aesthetically pleasing, pharmacologically effective, and demonstrated enhanced patient Compliance. They serve as a novel, natural, and convenient alternative to traditional dosage Forms, particularly beneficial for populations with swallowing difficulties.

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