

Formulation and Evaluation of Polyherbal gel for Management of Mouth Ulcer

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ABSTRACT:

The main purpose of this gel formulation of Guava leaves, Betel Leaves, Honey and Peppermint oil was to relieve pain and discomfort due to oral ulcers. As we know there are different types of ulcers in the mouth that cause inflammation and pain. The most common oral ulcers are Local trauma & Aphthous Stomatitis. Now many over-the-counter medications are essential to staying in primary healthcare because of the positive response and the most effective treatment with the least amount of side effects. Herbal medicines are still the backbone of almost 75-80% of the world's population, especially in developing countries, in primary healthcare due to better adherence to the human body, cultural acceptance and less side effects.

They are found mainly in tropical and subtropical regions of India, the Americas and Africa, where they occur in various countries. The gel contains the main ingredients Guava Leaves Powder, Betel Leaves powder, peppermint oil & Carbopol 934 as a gelling agent & and Propylene glycol as a co-solvent. Another ingredient Honey acts as an antiseptic. The formulated gel was tested for different parameters such as physicochemical parameters (pH, viscosity, Gel strength, etc.). The gel is homogeneous mixture that shows the pH 6.8. Developed herbal oral formulation was stable, safe and effective for treatment of mouth ulcer.0.1.

INTRODUCTION

An oral ulcer (also called a mouth ulcer or mucosal ulcer) is an ulcer that occurs in the mucous membranes of the mouth. They are painful round or oval ulcers that form in the mouth, especially inside the cheeks or lips. Mouth sores, also known as aphthous sores, can be painful when we eat, drink or brush our teeth. Common causes of mouth sores include a lack of nutrients like iron, vitamins especially B12 and C, poor oral hygiene, disease, depression, indigestion, mechanical damage, food intolerance, hormonal imbalance, skin disease etc. A mouth ulcer is a fracture or fracture of the mucous membrane, located in the middle of the mouth. It is usually yellow or white and usually looks like pressure on the mouth which is a mucous membrane. [1]



Fig.1.1

Gels are mainly semi-solid formulations having a liquid phase that has been thickened with some other components. Topical gel preparations are used for the skin application or percutaneous penetration of medicament or local action to certain mucosal surfaces. Herbal gel for oral care combines the goodness of nature with modern dental hygiene. Formulated with plant-derived ingredients, this innovative gel offers a holistic approach to maintaining oral health. Drawing upon the therapeutic properties of herbs, the gel provides a soothing and effective solution for various dental concerns. Infused with herbal extracts such as guava leaves betel leaves and honey, the gel promotes gum health, fights bacteria, and alleviates oral discomfort.^[2]

Guava leaves are often used in oral gels for their antimicrobial properties, which can help combat bacteria and reduce inflammation in the oral cavity. The leaves contain compounds like flavonoids and tannins that exhibit antibacterial and anti-inflammatory effects. ^[3]

Betel leaf extract is often used in oral gels due to its potential therapeutic properties. It's believed to have antimicrobial, anti-inflammatory, and antioxidant effects, which can contribute to Oral health. The extract may help in managing conditions like gingivitis and oral infections.^[4]

Honey can be used in oral gel formulations for its antimicrobial properties and wound-healing potential. It may help soothe and promotes healing in oral tissues. Additionally, honey's viscosity can contribute to the gel's texture, enhancing its adherence to oral surfaces. It's crucial to consider the concentration, type of honey, and compatibility with other ingredients in the formulation for optimal results. ^[5]

0.2 RATIONALE / HYPOTHESIS

Incorporation of herbal anti-bacterial agents in an herbal mouth ulcer gel could provide a safe and efficient mouth ulcer gel formulation.

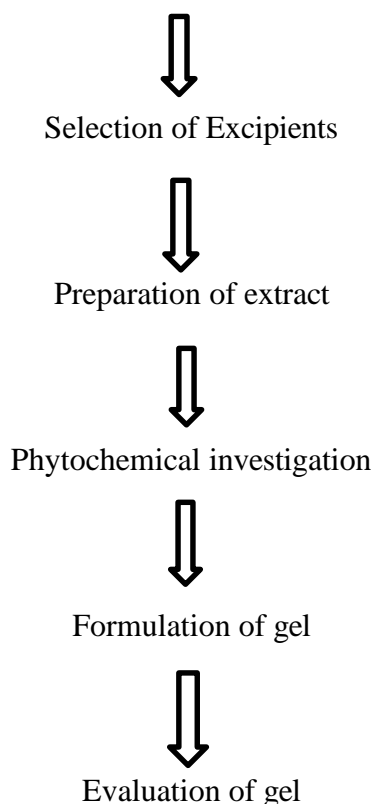
3.1 OBJECTIVES

1. To prepare herbal mouth ulcer gel to reduce pain and discomfort associated with mouth ulcer and prevent by utilizing natural ingredients known for anti-bacterial, anti-ulcer properties.
2. To evaluate the formulated herbal mouth ulcer gel for pharmacopeial standards and compare its efficacy with marketed formulation

3.2 PLAN OF WORK:

To achieve the set of objectives for the project, the work was divided into following section. Literature survey, Procurement of guava & betel leaves, honey, Selection of Excipient's, Extraction of guava & betel leaves, phytochemical investigation, Formulation of gel, Evaluation of gel

Literature survey



04. LITERATURE REVIEW

4.1. N. K. Jain *et al.*, (2020) reveal the selected herb guava leaves and betel leaves can be used for amelioration of symptoms and decreasing mouth ulcer due to cumulative antioxidant, antimicrobial, anti-inflammatory, analgesic and antiulcer properties.

4.2 S. Shaikh *et al.*, (2018) reveals that the Commercially available gels containing synthetic and semi synthetic active agents which have several disadvantages like staining on the teeth, irritation, and burning sensation only because presence of high degree of alcohol content and some organic compounds. The present investigation deals with use of herbal powdered Guava Leaves in the treatment of mouth ulcer in herbal gel.

4.3 V. Patil *et al.*, (2022) have the Psidium gujava leaf extract micro particles loaded gel is a good mucoadhesive gel for mouth ulcer management. Therefore, herbal ingredients can be used for novel drug delivery and make it safe for administration with lesser risk of adverse reactions.

4.4 Miss. H.B. Tribhuvan *et al.*, (2022) have the formulated gel was tested for different parameters such as physicochemical parameters such as pH, viscosity, distribution ability homogeneity, gel strength, clarity of gel ,etc. The gel is homogeneous mixture that shows the pH 6.8. This herbal gel was stable at room temperature protected from any germs and thus safe for use on mouth sores.

4.5 A. Pandit *et al.*,(2022)have antioxidant and antimicrobial properties of betel leaves(*piperbetle*). Ethanolic compounds extracted from betel leaf showed excellent anti-microbial activity against gram negative and gram-positive pathogens. The anti-bacterial activity of betel leaf is due to the presence of polyphenols.

4.6 Ranathunja K. et al.,(2022) reveal medicinal value, ethnomedicinal uses scientifically

validated biological activities, important phytochemicals, and Ayurveda properties regarding guava leaves (*Psidium guajava*). Survey of the literature revealed that *Psidium guajava* L. was a good source of health-promoting and contained secondary metabolites like Flavonoids, Tannins, glycosides, terpenoids, etc. The medicinal plant *Psidium guajava* L was re-ported to possess various pharmacological properties like antioxidant, anti-inflammatory, antimicrobial, ant cough.

4.7 V. Madaan *et al.*, (2022) have detail information about mechanism of action of honey. Honey is antibacterial and anti-inflammatory properties so it apply on mouth ulcer so it decrease the inflammation and also kill bacteria in mouth so decrease inflammation in so automatically healing ulcer.

4.8 Ranathunja K. et al.,(2022)reveal medicinal value, ethnomedicinal uses scientifically validated biological activities, important phytochemicals, and Ayurveda properties regarding guava leaves (*Psidium guajava*). Survey of the literature revealed that *Psidium guajava* L. was a good source of health-promoting and contained secondary metabolites like Flavonoids, Tannins, glycosides, terpenoids, etc. The medicinal plant *Psidium guajava* L was re-ported to possess various pharmacological properties like antioxidant, anti-inflammatory, antimicrobial, anticough.

4.9 R. sing *et al.*, (2020) gives good antimicrobial, antifungal, anticancer activity of Guava. some essential phytoconstituents such as tannins, triterpenes, flavonoid, quercetin, pentacyclic triterpenoid, guajanoic acid, Saponin, carotenoids, lectins, leucocyanidin, ellagic acid, amritoside, beta-sitosterol, uvaol, oleanolic acid and ursolic acid.

4.10 N. Shahare *et al.*, (2021) have prepared and evaluated mouth ulcer gel formulation using betel leaves as one of the ingredients. The leaves show various pharmacological activities like antiulcer, antibacterial, antifungal, anti- inflammatory, antioxidant activities.

05. EXPERIMENTAL

5.1. DRUG AND EXCIPIENT PROFILE

5.1.1. Guava leaves



Fig .5.1

Synonyms:

Peru, Jaam, Amrood.

Biological source:

It is dried leaves of *Psidium guajava* L. belonging to the family Myrtaceae.

Geographical source:

Guava is native to tropical America and seems to have been growing from Mexicoto Peru. It is also cultivated in India, Indonesia, Pakistan, and Bangladesh.

Chemical Constituent:

It contains important phytoconstituents such as tannins, triterpenes and flavonoid, quercetin, pentacyclic triterpenoid, guajanoic acid, saponin, carotenoid, lectins, leucocyanidin, ellagic acid, amritoside, uvaol, oleanolic acid and ursolic acid

Uses:

Antiulcer, antimicrobial, anti-inflammatory, antioxidant.

5.1.2 Betel leaves

Fig.5.2

Synonyms:

betelvine, betlepepper, pan.

Biological source:

It is dried leaves of *piper betle* belonging to family Piperaceae.

Geographical source:

It is cultivated mostly in South and Southeast Asia. It is also cultivated in India, Srilanka, Thailand and Bangladesh.

Chemical Constituents:

Plant contains aterpinine, P-cymene, carvacrol, chavicol and its derivatives, allylcatechol, eugenol, estragol, oxalic acid, malic acid and amino acids. Leaves contain good amounts of vitamins particularly nicotinic acid, ascorbic acid and carotin. They also contain significant amounts of all essential amino acids except lycine, histidine and arginine.

Uses: Antibacterial, Antiseptic, Antiulcer, Anti-inflammatory.

5.1.3.Honey

Fig.5.3

Synonyms

Madhu, Madh, Mel, Purified Honey

Biological Source:

Honey is a viscid and sweet secretion stored in the honey comb by various species of bees, such as *Apis mellifera*, *Apis dorsata*, *Apis florea*, *Apis indica* and other species of *Apis*, belonging to family Apidae (Order: Hymenoptera).

Geographical Source:

Honey is available in abundance in Africa, India, Jamaica, Australia, California, Chili, Great Britain and New Zealand.

Chemical Constituents:

Moisture 14–24%, Dextrose 23–36%, Levulose (Fructose) 30–47%, Sucrose 0.4–6%, Dextrin and Gums 0–7% and Ash 0.1–0.8%. Besides.

It is found to contain small amounts of essential oil, bees wax, pollen grains, formic acid, acetic acid, succinic acid, maltose, dextrin, coloring pigments, vitamins and an admixture of enzymes.

Uses:

Honey shows good antimicrobial, anti-inflammatory, anti-pyretic activity and gives the soothing effect to the skin.

5.1.4. Peppermint Oil

Fig.5.4

Synonyms:

Menta Piperita

Biological Source:

Peppermint oil is the essential oil taken from the flowering parts and leaves of the peppermint plant

Chemical constituents:

The chief constituent of Peppermint oil is Menthol, along with other constituents like methyl acetate, isovalerate, menthone, cineol, in active pinene, limonene, and other less important bodies. The English oil (60 to 70%), the Japanese oil (85%), and the American (50%) of Menthol

Uses:

Relieve pain, Kill germs, Boost blood circulation.

5.1.5. Carbopol 934

Fig.5.5

Chemical Formula:

C₅H₁₀O₂

Physical Properties:

It is Fine, white, fluffy powder that insoluble in water; swells to form a gel when dispersed in water

Uses:

Carbopol 934 is commonly used as a thickening agent in various pharmaceutical formulations, such as gels, creams, and lotions.

It helps to improve the viscosity and consistency of topical medications, enhancing their

5.1.6. Methyl paraben

Fig. 5.6

Chemical Formula:

C₈H₈O₃

Physical properties:

Methyl paraben is a white, odorless crystalline powder with a slightly bitter taste. It is soluble in alcohol and ether, but only slightly soluble in water.

Uses:

Methyl paraben is commonly used as a preservative in cosmetics, personal care products, pharmaceuticals, and food. It helps prevent the growth of bacteria, fungi, and other microorganism.

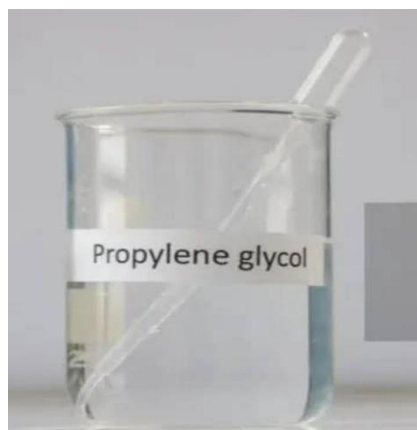
5.1.7. Propyl paraben

Chemical Formula:C₁₀H₁₂O₃**Fig.5.7****Physical properties :**

Propyl paraben appears as white crystalline Powder. It is soluble in alcohol, ether, and propylene glycol, but only slightly soluble in water.

Uses:

Propyl paraben is commonly used as a preservative in cosmetics, pharmaceuticals, and food products to prevent the growth of bacteria, mold, and yeast

5.1.8 Propylene glycol**Fig.5.8****Chemical Formula:**C₃H₈O₂**Physical properties:**

Propylene glycol is a colorless, odorless and slightly viscous liquid.

Uses:

Propylene glycol is commonly used as a solvent in pharmaceuticals and as a humectant in cosmetics and personal care products. Additionally, it's utilized as a food additive to maintain moisture and texture.

5.1.9. Triethanolamine**Fig no. 5.9**

Chemical Formula:

C₆H₁₅NO₃

Physical Properties:

TEA is a viscous, colorless liquid with a slight ammonia-like odor. It's highly soluble in water and miscible with ethanol, ether, acetone, and chloroform.

Uses:

TEA is used as an emulsifier, surfactant and pH adjuster in products

5.2 MATERIALS AND RESEARCH METHODOLOGY

5.2.1 MATERIALS & EQUIPMENTS

5.2.1.1 List of Drugs:

Drug and materials used in dissertation work is listed in Table 5.1 along with their supplier. Table 5.1: List of drugs used in dissertation work

Sr.No.	Drugs	Particulars
1.	Guava Leaves	Kolhapur Locality
2.	Betel Leaves	Kolhapur Locality
3.	Honey	Kolhapur Locality
4.	Peppermint Oil	Unique biology Shahupuri, Kolhapur
5.	Carbopol 934	Unique biology Shahupuri Kolhapur
6.	Methyl paraben	Unique biology Shahupuri Kolhapur
7.	Propyl paraben	Unique biology Shahupuri Kolhapur
8.	Propylene glycol	Unique biology Shahupuri Kolhapur
9.	Triethanolamine	Unique biology Shahupuri Kolhapur

Tab.5.1

5.2.1.2. List of Materials:

Materials used in dissertation work is listed in Table 5.2 along with their manufacturers. Table 5.2: List of materials used in dissertation work

Sr.No.	Material	Manufacturer
1.	Stirrer	Unique biology Shahupuri Kolhapur
2.	Pair of Tongs	Unique biology Shahupuri Kolhapur
3.	Beakers	Unique biology Shahupuri Kolhapur
4.	China Dish	Unique biology Shahupuri Kolhapur
5.	Container	Unique biology Shahupuri Kolhapur

Tab.5.2

5.2.1.2. List of Equipment :

Equipment used in dissertation work is listed in Table 5.3 along with their manufacturers. Table 5.3: List of equipment used in dissertation work

Sr.No.	Equipment	Manufacturer
1.	Digital weighing balance	CONTECH , India
2.	Thermostat Water bath	Bio techniques, India
3.	Digital pH meter	J-SIL ,India
4.	Brookfield Viscometer	Coslab Pvt. Ltd. ,India
5.	Magnetic Stirrer	Coslab Pvt. Ltd. ,India

5.2.2. RESEARCH METHODOLOGY

5.2.2.1. Preparation of Extract : Methods used for Extraction:

Sr. No.	Plant	Method of Extraction	Solvent
1	Psidium guajava	Soxhlet extraction	Methanol
2	Piper betle	Maceration	Ethanol

Tab.5.4

5.2.2.2. Phytochemical Investigation:



1. Test for Alkaloid
2. Test for Flavonoid
3. Test for Glycosides
4. Test for Saponin
5. Test for Triterpenoids

6. Test for Terpenoid

5.2.2.3. Method of Preparation:

- Carbopol 934 dispersed into distilled water.
- Add methyl paraben and propyl paraben in distilled water.
- Heating on water bath.
- Add propylene glycol aftercooling
- Then add different concentration of leaves powder.
- At last full mixed ingredients added in Carbopol 934 gel with properly.
- Continuous stirring add triethanolamine drop wise for adjust pH (6.8-7).

5.2.2.4. Formulation table:

Table 5.5 : Composition of various gel formulations.

Sr. No.	Ingredients	F1	F2	F3	F4	F5
1.	Guava Leaves	0.03	0.3	0.6	0.9	1.2
2.	Betel Leaves	0.15	1.5	3	4.5	6
3.	Honey	2	2	2	2	2
4.	Peppermint Oil	0.01	0.01	0.01	0.01	0.01
5.	Carbopol934	0.3	0.3	0.3	0.3	0.3
6.	Methyl paraben	0.06	0.06	0.06	0.06	0.06
7.	Propyl paraben	0.03	0.03	0.03	0.03	0.03
8.	Propylene glycol	1.5	1.5	1.5	1.5	1.5
9.	Triethanolamine	0.36	0.36	0.36	0.36	0.36
10.	Distilled water	Up to 30	Up to 30	Up to 30	Up to 30	Up to 30

Tab.5.5

Evaluation Test:

I. Physical Evaluation:

Physical parameters such as color, odour and consistency were checked visually

II. Measurement of pH:

The pH of gel formulation were determined by using digital pH meter. Take 1gm of gel and dissolved in 10 ml of distilled water and keep apart for two hours. Then the measurement of pH of formulation was done by dipping the glass electrode completely into the gel system three times and the average values are reported [9]. The pH of gel formulation was reported. [6]

III. Homogeneity :

All prepared gel formulation were tested for homogeneity by visual inspection after the gels have been set in to the container. They were tested for their presence and appearance of any aggregates. Homogeneity of gel formulation was reported. [7]

IV. Viscosity :

The measurement of viscosity of the formulated gel was determined by Brookfield Viscometer with spindle no. 1 at 25°C. The gels were rotated at speed 1.5 rotations per minute and at each speed, the corresponding dial reading was noted. Then viscosity of the prepared gels were obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer catalogues [8] Viscosity of gel formulation was reported.

V. Spreadability :

Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel that is placed in between the slides under the direction of certain load. If the time taken for separation of two slides is less then better the spreadability [9]. Spreadability is calculated by using the formula:

$$S = M \times L / T$$

Where M=weight of to upper slide

L = length of glass slides

T = Time taken to separate the slides

Spreadabilty of gel Formulation were reported.

VI. Clarity :

The clarity of formulation was determined by visual inspection. [10].

VII. Gel strength:

Gel strength was determined by the time in seconds required by the weight to penetrate in the gel. A 3.5 gm weight was placed on the surface of 5 gm formulated gel. Gel strength was determined by reporting the time in seconds required by the weight to penetrate 0.5cm in the gel[7].The gel strength was then reported.

VII. Anti-bacterial activity:

The anti-bacterial activity of preparation was performed against Gram-positive (Staphylococcus aureus NCIM5021,)and Gram-negative (E.coli NCIM 2832) bacteria by modified agar well diffusion method.[1,3] The suspension of test pathogens was prepared in sterile saline and used for further study. For the anti-bacterial activity test pathogens were inoculated on the surface of sterile nutrient agar plates and spread on plates by using a sterile spreader in an aseptic condition. After that agar well was prepared aseptically with the help of a sterilized glass cork borer having a 0.7 cm

diameter. Then 100 µl volume of the test sample was added in the different wells of the respective test pathogens. Then plates were placed at 4°C for 20 min for sample diffusion in a culture medium and transferred to an incubator at 37°C for 24 hrs. Furthermore, the obtained results were compared with the well containing 1000 µg /ml Streptomycin as a positive control.[11] The diameter of the inhibition zone was measured in mm and the results were recorded (Table 6.3).

06. RESULT AND DISCUSSION:

6.1. Result:

Table 6.1 :Phytochemical Investigation

Sr. No.	Secondary Metabolites	Methanolic extract of P. guajava leaf	Ethanollic extract of P. Betle leaf
1	Alkaloid	+	+
2	Flavonoid	+	-
3	Polyphenols	+	+
4	Saponins	+	-
5	Triterpenes	+	-
6	Tannins	+	+

Tab.6.1

I. Physical evaluation:

Table.6.2:Physical test for gel formulation

Sr.No.	Parameters	Observations
1.	Nature	Semi-solid
2.	Color	Brownish
3.	Odour	Characteristics
4.	Texture	Smooth

Tab.6.2

II. pH :

Using pH meter the pH of formulation was found to be 6.77.

III. Homogeneity:

By visual inspection the Homogeneity of gel formulation was found to be good.

IV. Viscosity:

The viscosity of the formulation was measured by using Brookfield viscometer.

Sr. No.	Batch No.	Viscosity in Cps
1.	F2	47200

Tab.6.3

V. Spreadability:

Spreadability investigations revealed that formulation have greater spreadability. It was found to be 17.98 Gm.cm/sec.

VI. Clarity:

The clarity of formulation was determined by visual inspection. It was found to be clear.

VII. Gel strength:

Gel strength of formulation was found to be 36±0.07 sec.

VIII. Anti-bacterial activity :

Obtained results states that the gel shows good anti-bacterial activity against test pathogens which are

mainly involved in mouth infections.

Table no.6.3 Anti-bacterial activity of the formulated gel against respective test pathogens in

Sr. No.	Test organisms	Zone of inhibition in mm		
		Finished Product	Base	Streptomycin
1.	S. aureus	24	00	30
2.	E. coli	22	00	31

Tab.6.4



Fig 6.1. Anti-bacterial activity against Staphylococcus aureus



Fig .6.2 Anti-bacterial activity against Escherichia coli

6.2. DISCUSSION:

From the result it is clearly shown that the prepared gel formulations having good homogeneity and gelling properties. The pH of all gel formulations was in the range of compatible with normal pH range of the skin. The spreadability shows that with increasing viscosity of formulation, spreadability decreases and vice versa. The gelling strength of the batch was found in the suitable range. The batch of developed formulation showed anti-bacterial activity against Staphylococcus aureus and Escherichia coli this are main microorganism responsible for mouth ulcer and formulation it can also use to treat mouth ulcer infection.

07. SUMMARY & CONCLUSION

From the mentioned results, it was concluded that the prepared gel formulations are in good appearance

with suitable pH range. Formulated gel have good homogeneity, proper gel strength & spread ability. The gel is neither too thick nor too thin. The all-formulated gels are found to best able in closed container compared to open container. The formulation showed the antibacterial and antiulcer activity against *Staphylococcus aureus* and *Escherichia coli*.

Therefore, the study concluded that the herbal products are more acceptable & they are safer with minimum side effects than synthetic prepositions.

Thus, the data presented in this study, it was concluded that the formulated gel of powdered Guava Leaves, Betel Leaves and honey with peppermint oil possesses a significant therapeutically efficacious & have suitable vehicle for drug delivery.

Thus, the formulated gel is found to be suitable for treatment of mouth ulcer.

08. FUTURE SCOPES :

The future scope of herbal mouth gels appears promising, driven by increasing consumer interest in natural and holistic healthcare products. Here are several key areas where herbal mouth gels may see significant growth and development:

Rising Demand for Natural Products: Consumers are increasingly leaning towards natural and organic products due to concerns about synthetic chemicals and their side effects. Herbal mouth gels, which typically use natural ingredients like neem, clove, aloe Vera and tea tree oil, align with this trend and are perceived as safer and more eco-friendly alternatives to conventional oral care products.

Health Benefits and Efficacy: There is growing scientific evidence supporting the efficacy of herbal ingredients in promoting oral health. Studies have shown that certain herbs possess antibacterial, anti-inflammatory, and antioxidant properties, which can help prevent dental issues like cavities, gum disease, and bad breath.

Holistic Health and Wellness Trends: As the holistic health and wellness movement grows, products that offer comprehensive health benefits, including oral health are becoming more popular. Herbal mouth gels that emphasize overall well-being and connect oral health with general health may attract a broader audience.

In conclusion, the future scope of herbal mouth gels is bright, with opportunities for growth driven by consumer preferences for natural products, ongoing scientific research, regulatory advancements, and innovations in product formulation, market expansion, sustainability trends, and the integration of digital health technologies.

REFERENCES:

1. Richa Sing*, Sagar Bansal and Manoj Kumar Mishra; Formulation and Evaluation of Herbal Oral Gel Containing Extracts of Powdered *Psidium guajava* Linn Leaves with *Curcuma longa* Linn Rhizomes to Treat Mouth Ulcer, International Journal of Drug Development and Research, 2020, vol 12.
2. Singh M, Mittal V (2014) Formulation and evaluation of herbal gel containing ethanolic extract of *Ipomoea fistulosa*. Int J Sci Res. 3: 1862-1866.
3. Mital Kaneria, Sumitra Chanda,(2011) Phytochemical and Pharmacogenetic Evaluation of leaves of *Psidium Guajava* L. (Myrtaceae), Pharmacognosy Journal, , 3(23), 41-45.
4. Sengupta R and Banik JK (2013) : A review on betel leaf (pan). Int J Pharm Sci Res; 4(12): 4519-24.
5. Molan P (1999): Why honey is effective as a medicine. 1. Its use in modern medicine. Bee World 80:79-92,

6. Mokashi M (2015) & formulation and evaluation of Herbal Gel Containing Methanolic Extract of *Annona squamosa* Leaves, *Int JSci Res.* 4: 1064-1065
7. Thombre KP, Sharma D, Lanjewar AM (2018) & formulation and evaluation pharmaceutical aqueous gel of powdered cordia dichotoma leaves with guava leaves. *Am J Pharm Tech Res.*8: 269-274.
8. Yogi D (2015) & formulation and evaluation of gel containing amlexanox for mouth ulcer. *Int J Appl Pharm. Biol Res.* 4:356-364.
9. Kaur LP, Garg R, Gupta GD (2010) Development and evaluation of topical gel of minoxidil from different polymer bases in application of alopecia. *Int J Pharmacy Pharm Sci.*2: 43-47.
10. Pandey N (2011) formulation and evaluation of invitro Antimicrobial activity of gel containing essential oils and effect of polymer on their antimicrobial activity. *Int J Pharm and Pharmaceut Sci* 3: 234-238.
11. Vidya V, Aleykutty NA, Jayakar B, Subin MZ. Development and evaluation of antimicrobial herbal formulations containing the methanolic extract of *Samadera indica* for skin diseases. *J Adv Pharm Technol Res.* 3 (2); 2012: 106-111.
12. Muruganandam L, Anantha Krishna, Jashwanth Reddy, G.S. Nirmala, (2017), Optimization studies on extraction of phytocomponents from betel leaves, *Resource-Efficient Technologies* doi: 10.1016/j.reffit.2017.02.007
13. Guha, P .(1997) “Paan Theke Kutir Silpa Sambhabana” (In Bengali). “Exploring Betel Leaves for Cottage Industry”, In: *Krishi, Khadya-O- Gramin Bikash Mela –A Booklet* published by the Agricultural and Food Engineering Department, IIT, Kharagpur, India; 15-19.
14. Satyavati GV, Raina MK, Sharma M. (1987) *Medicinal Plants of India*. New Delhi: Indian Council of Medical Research, New Delhi, India. Vol 1.