



FORMULATION AND EVALUATION OF HERBAL ORAL GEL CONTAINING EXTRACTS OF POWDERED *PSIDIUM GUAJAVA* LINN LEAVES WITH *CURCUMA LONGA* LINN RHIZOMES TO TREAT MOUTH ULCER

Richa Singh¹, Sagar Bansal², Manoj Kumar Mishra³

^{1,2,3}Department of Pharmaceutics, Shambhunath Institute of Pharmacy, Jhalwa, Prayagraj – 211012, (U.P.), India.

*Corresponding author E-mail: richasingh13may@gmail.com

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ABSTRACT

The objective of this study was to formulate and evaluate the herbal oral gel containing extracts of powdered *Psidium guajava* Linn leaves and *Curcuma longa* Linn rhizomes to treat mouth ulcer. The traditional medical study is an integral part of the culture and the interpretation of health by indigenous populations in almost world. Guava leaves have been usually used to govern several diseases such as rheumatism, diarrhea, diabetes mellitus, wound sore throat, cough and it also gives good antimicrobial, antifungal, anticancer activity. Guava contains various essential phytoconstituents such as flavonoid: quercetin, saponins, pentacyclic triterpenoid: guajanoic acid, tannins, triterpenes, ellagic acid, amritoside, beta-sitosterol, uvaol, carotenoids, lectins, leucocyanidin, oleanolic acid and ursolic acid while turmeric has anti-inflammatory, antibacterial activity, virucidal, antimutagenic, antioxidant properties. Turmeric contains a large variety of phytochemicals such as curcumin, demethoxycurcumin, eugenol, tannins, alkaloids, saponins, terpenoids and curcumol. The herbal oral gel formulation was prepared by using guava leaf extract, turmeric rhizome extract, carbopol 934, propylene glycol, methyl paraben, propyl paraben, triethanolamine and required amount of distilled water. The triethanolamine was added drop wise to maintain the pH (6.7-7.2) of oral mucosa. The physicochemical parameters of formulations such as pH, spreadability, viscosity, extrudability, gelling strength and antifungal activity were determined. The results showed that the optimized herbal oral formulation containing guava leaf extract and turmeric rhizomes extract shows that all physicochemical parameters were found to be compatible with the normal range. Anti-fungal study of formulation revealed excellent efficacy against *Candida albicans*. Formulated herbal oral gel was stable, safe and effective for the treatment of mouth ulcer.

INTRODUCTION:

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 surfaces¹. Mouth ulcers are small sores or an abrasion that develops in mouth or at the base of gum. Mouth ulcers are also known as canker sores or aphthous ulcer. A break or breach in the

mucous membrane, that lines within the mouth is also recognised as a mouth ulcer. It generally arises as a yellow or white colour depression in mouth. Mouth ulcers are usually generated by a number of causes, such as biting the inner layer of cheek, food allergies, hard teeth brushing, hormonal changes, vitamin deficiencies, bacterial infection and diseases².



Figure 1: Mouth ulcer

Over three fourth of world population depends mainly on the plants and plant derived herbal medicines. 30 % of the plant species are used for medicinal purposes. Market for plant derived drugs of whole world may estimate for about Rs. 200,000 crores. Presently, contribution of India is less than Rs. 2000 crores. Export of raw drugs from India has gradually grown by 26% to Rs. 165 crores in 1994-95 from Rs. 130 crores in 1991-92. The yearly production of raw material from medicinal and aromatic plants is worth about Rs. 200 crores. This is likely to reach US \$1150 by the year 2000 and US \$5 trillion by 2050³. It has been observed that plant drugs constitute 25% of total drugs in developed countries such as United States, while in fast developing countries like China and India the contribution is above 80%. Thus, the economic importance of medicinal plants in India is much more than rest of the world. These countries contributes two third of the plants used in modern system of medicine and the indigenous systems of medicine provides health care system of rural population⁴. *Psidium guajava* L. is also known as Guava. It is a medicinal plant belongs to the family Myrtaceae and widely distributed throughout India. Guava (*Psidium guajava* L.) leaves have traditionally been used to manage several diseases such as rheumatism, diarrhea, diabetes mellitus, wound sore throat, cough and it also gives antibacterial activity, anticancer activity. It contains various essential phytoconstituents such as flavonoid:

quercetin, saponins, pentacyclic triterpenoid: guajanoic acid, tannins, triterpenes, ellagic acid, amritoside, beta-sitosterol, uvaol, carotenoids, lectins, leucocyanidin, oleanolic acid and ursolic acid⁵.



Figure 2: Guava leaves and fruits

The biological source of turmeric is *Curcuma longa* that belongs to the family Zingiberaceae. There are some important phytochemical components of turmeric include diaryl heptanoids, a class including several curcuminoids, such as curcumin, demethoxycurcumin, and bisdemethoxycurcumin. Due to presence of volatile oils turmeric possess anti-inflammatory and anti-arthritic activities. Water and fat soluble extracts of curcumin showed strong antioxidant activity comparable to vitamins C and E⁶.



Figure: 3 Turmeric plant, rhizomes and powder

The aim of present study is to establish the Formulation and Evaluation of herbal oral gel containing extracts of powdered *Psidium guajava* Linn leaves and *Curcuma longa* Linn rhizomes to treat mouth ulcer

MATERIALS AND METHODS

Collection and authentication of Plant materials

The leaves of plant *Psidium guajava* and rhizomes of *Curcuma longa* were collected from the local area of Jhalwa, Prayagraj, Uttar Pradesh, India in month of September 2019 and the plant specimens are authenticated by "BOTANICAL SURVEY OF INDIA, PRAYAGRAJ" Accession no. 104331 and 104332 respectively.

Chemicals

Ethanol, Methanol, Carbopol 940, Methyl paraben, Propyl paraben, Propylene glycol 400, Triethanolamine, Distilled water. All ingredients of analytical grade purchased from Merk Ltd and Thomas Baker chemical pvt. Ltd.

Equipments

Digital balance, pH meter, Magnetic stirrer, Digital water bath, Ultra sonicator, Brookfield LVDV – II + Pro viscometer.

PREPARATION OF PLANT EXTRACTS

The leaves of guava and rhizomes of turmeric were washed under running tap water to remove dust particles and shade dried at room temperature for 3-4 weeks. The dried plant parts were reduced to coarse powder with a mechanical grinder and passed through a 40 no. mesh sieve. The powder was then subjected to extraction by cold maceration using ethanol, methanol and water to attain their respective extracts. Both 100 g of dried guava leaves powder and turmeric powder were macerated in 500 ml of ethanol, methanol and water in separate conical flask for 24 hrs at room temperature, under occasional shaking. After 24 hrs mixtures were filtered out using simple filtration method and filtrates were collected in separate vessels. To obtain the extract the solvent were removed from the filtrate under reduced pressure by using a rotary vacuum evaporator at 45- 50°C⁷.

PREPARATION OF HERBAL GEL

Take 15 ml of distilled water in a beaker and disperse specified amount of

carbopol 940 in it with continuous stirring. Keep the beaker aside to swell the carbopol for half hour. In another beaker take 5 ml of distilled water and add required quantity of methyl paraben and propyl paraben to it by heating on water bath. Cool the solution, then add Propylene glycol 400. Further required quantity of extract was added to the above mixture and this solution was mixed properly to the Carbopol 940 gel with continuous stirring. finally volume made up to 30 ml by adding remaining distilled water and triethanolamine was added drop wise to the formulations for adjustment of required mouth skin pH (6.8-7) and to obtain the gel at required consistency. The same method was followed for preparation of control sample without adding any extract⁸.

FORMULATION TABLE

The method describes above and the formulae were tabulated in Table no. 1. Along with control sample gel were prepared by addition of required quantity of *Psidium guajava* leaves extract and *Curcuma longa* rhizomes extract to prepared 1%, 2% and mixed mouth ulcer gel respectively⁸.

EVALUATION PARAMETERS:

1. Physical evaluation

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

- **Colour:** The color of the formulations was checked by visual inspection.
- **Consistency:** The consistency of formulations was checked by applying on skin.
- **Odour:** The odour of the formulations was checked by mixing the gel in water and observing the smell.

Physical evaluations of gel formulations were reported in table no. 2.

2. Percentage yield

Firstly take the weight of empty container in which the gel formulation was stored then again weigh the container with gel formulation. To obtain the practical yield subtract the weight of empty container with the container with gel formulation. Then the percentage yield was calculated by the formula given below:

Percentage yield = (Practical yield / Theoretical yield) × 100

Percentage yield of gel formulations were reported in table no. 3.

3. Measurement of pH

Digital pH meter was used for the measurement of pH of gel formulations. Take 1 gm of gel and dissolved in 10 ml of distilled water and keep apart for two hours. Then the measurement of pH of formulations was done by dipping the glass electrode completely into the gel system three times and the average values are reported⁹. The pH of gel formulation was reported in table no. 4.

4. Homogeneity

All prepared gel formulations 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 aggregates¹⁰. Homogeneity of gel formulation was reported in table no 5.

5. 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 0.3, 0.6 and 1.5 rpm and the corresponding dial reading was noted at each speed. Then viscosity of the prepared gels was obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer catalogues¹¹. Viscosity of gel formulation was reported in table no. 6.

6. Spreadability

Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel which is placed in between the two slide under the direction of certain load. If the time taken for separation of two slides is less then better the spreadability¹². Spreadability is calculated by using the formula:

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

Where,

M = Weight tied to the upper slide

L = Length of glass slides

T = Time taken to separate the two slides

Spreadabilty of gel formulations were reported in table no. 7.

7. Extrudability

Prepared gel were filled in different standard capped collapsible aluminium tubes and sealed by crimping at the end. The weight of filled tubes was recorded and the tubes were sandwiched between two glass slides and were clamped. 500gm weight was placed over the slides and then the cap was removed to extrude. The amount of extruded gel was collected and weighed. Extrudability was determined by calculating the percentage of extruded gel.

1. Extrudability is excellent when it is greater than 90%.

2. Extrudability is good when it is greater than 80%.

3. When it is 70% then extrudability is fair¹³

Extrudability of gel formulations were reported in table no. 8.

8. Clarity

The clarity of all the three batches was determined by visual inspection¹⁴.

9. Gel strength

Gel strength was obtained 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 0.5 cm in the gel¹⁰. The gel strength was then reported in table no 9.

10. Antifungal activity

The antifungal activity of all optimized formulation and blank formulation were carried out by Cup-plate method in comparison with marketed antifungal formulation (Daktarin oral gel). The antifungal activity test was performed by using Candida Albicans. Prepared nutrient brought and poured in to sterile petri plates and kept aside for drying and cooling. After that candida albican culture were spread by micron wire loop. Then 4 mm deep three holes are bored in the petridish using a sterile cork borer of 6 mm diameter then place 0.5 gm of gel from each formulation in to these holes and then incubate the plates at 27°C for 48 hr. Then the zone of inhibition (diameter in mm) was measured^{15, 16}.

Antifungal studies were reported in table no. 11.

RESULT AND DISCUSSION

Table no. 1: Composition of various gel formulations

Ingredients	Quantity in gm or ml				
	F1 (1%)	F2(2%)	F3(1%)	F4(2%)	F5(Mixed)
Guava leaf extract	0.30	0.60	-	-	0.45
Turmeric rhizome extract	-	-	0.30	0.60	0.45
Carbopol 940(1%)	0.30	0.30	0.30	0.30	0.30
Methyl paraben(0.2%)	0.06	0.06	0.06	0.06	0.06
Propyl paraben(0.1%)	0.03	0.03	0.03	0.03	0.03
Propylene glycol 400(5%)	1.5	1.5	1.5	1.5	1.5
Triethanolamine(1.2%)	0.36	0.36	0.36	0.36	0.36
Glycerine(1.5%)	0.45	0.45	0.45	0.45	0.45
Distilled water	Up to 30 ml	Up to 30 ml	Up to 30 ml	Up to 30 ml	Up to 30 ml

1. Physical evaluation

Table no. 2: Physical evaluation of gel formulations

Formulations	Color	Consistency	Odour
F 1	Yellowish green	Good	Characteristic
F 2	Yellowish green	Good	Characteristic
F 3	Yellowish green	Good	Characteristic
F 4	Yellowish green	Good	Characteristic
F(mixed)	Yellowish green	Good	Characteristic

Percentage yield

Table no. 3: Percentage yield of gel formulations

Formulations	Percentage yield (%)
F 1	96.985
F 2	98.110
F 3	95.421
F 4	96.992
F(mixed)	98.876

pH

Table no. 4: pH of gel formulations

Formulations	pH
F 1	6.9
F 2	7.1
F 3	7.0
F 4	6.9
F(mixed)	6.8

Homogeneity

Table no. 5: Homogeneity of gel formulations

Formulations	Homogeneity
F 1	Good
F 2	Good
F 3	Good
F 4	Good
F(mixed)	Good

Viscosity

Table no. 6: Viscosity of gel formulations

Formulations	Viscosity(cps)
F 1	4800
F 2	4800
F 3	4900
F 4	4700
F(mixed)	4500

Spreadability

Table no. 7: Spreadability of gel formulations

Formulations	Spreadability (gm.cm/sec)
F 1	29.60
F 2	29.12
F 3	24.51
F 4	31.90
F(mixed)	33.20

Extrudability

Table no. 8: Extrudability of gel formulations

Formulations	Extrudability(%)
F 1	78.0
F 2	79.0
F 3	77.5
F 4	87.0
F(mixed)	89.5

Gelling strength

Table no. 9: Gelling strength of gel formulations

Formulations	Gelling strength
F 1	41±0.15
F 2	39±0.10
F 3	35±0.24
F 4	28±0.75
F(mixed)	26±0.12

Table no. 10: Optimization of batches

Parameters	Optimized batch F(mixed)
Color	Yellowish green
Odor	Characteristics
pH	6.8
Viscosity	4500
Spredabilty	33.20
Extrudability	89.5
Gelling strength	26±0.12

Anti fungal studies

Table no. 11: Antifungal studies of gel formulations

Formulations	Zone of inhibition (mm)
	Candida albicans
Standard drug	27
F(mixed)	24
Blank	14



Figure: 4 Zone of inhibition
Stability studies

Table no. 12: Stability study at 25⁰C temperature 60%± 5% RH

Evaluation parameters	F(mixed)		
	Month-1	Month-2	Month-3
Color	Yellowish green	Yellowish green	Yellowish green
pH	6.8	6.8	6.8
Viscosity	4500	4500	4500
Spreadability	33.18	33.18	33.17
Extrudability	89.4	89.5	89.4
Gelling strength	26±0.10	26±0.11	26±0.11

Table no. 13: Stability study at 30⁰C temperature 65%± 5% RH

Evaluation parameters	F(mixed)		
	Month-1	Month-2	Month-3
Color	Yellowish green	Yellowish green	Yellowish green
pH	6.8	6.8	6.8
Viscosity	4500	4500	4500
Spreadability	33.19	33.18	33.18
Extrudability	89.4	89.4	89.5
Gelling strength	26±0.10	26±0.11	26±0.11

Table no. 14: Stability study at 40⁰C temperature 75%± 5% RH

Evaluation parameters	F(mixed)		
	Month-1	Month-2	Month-3
Color	Yellowish green	Yellowish green	Yellowish green
pH	6.8	6.8	6.8
Viscosity	4500	4500	4500
Spreadability	33.18	33.19	33.19
Extrudability	89.4	89.4	89.5
Gelling strength	26±0.11	26±0.10	26±0.11

11. Stability study

Stability studies were performed to observe the effect of environmental conditions or storage conditions on formulation. The optimized formulation was kept in accelerated stability condition at 25°C temperature 60± 5% relative humidity, 30°C temperature 65±5% relative humidity and 40°C temperature 75±5% for a period 3 months as per ICH guidelines. The placed sample was withdrawn at 1, 2 and 3 months interval and evaluation was carried out for physical appearance, pH, viscosity, spreadability, extrudability and gelling strength¹⁷. Stability study was reported in table no.12, 13, 14 .

Optimization of batches:

After analysis of all batches of formulations for their evaluation parameters like pH, viscosity, spreadability, extrudability and gelling strength it is observed that the formulation F (mixed) containing equal amount of guava leaf extract and turmeric rhizome extract showed good result. The batch F (mixed) optimized with good pH, viscosity, spreadability, extrudability and gelling strength, hence this formulation is further used for anti fungal study. From the above results it is clearly shows that all the prepared gel formulations was yellowish green in color and having good homogeneity and gelling property. The pH of all gel formulations was in the range compatible with normal pH range of oral cavity. The rheological behaviors of gel formulations were studied with Brookfield viscometer which indicated that the viscosity of gel formulation was consistent neither too thick nor too thin. The study of spreadability shows that with increasing the viscosity of formulation spreadability decrease and its vice-versa. The gelling strength and extrudability is found in the suitable range. Thus overall, the gel formulation F (mixed) complies with all parameters of an ideal gel. Accelerated stability studies indicated that the physical appearance, rheological properties, extrudability, spreadability in the optimized formulation remain unchanged upon storage for 3 months. F (mixed) formulation showed good anti-inflammatory and antifungal activity against *Candida albicans* that is main microorganism responsible for mouth ulcer.

CONCLUSION

Natural remedies are more acceptable in the belief that they are safer with lesser side effects than the synthetic medicines. Nowadays herbal formulations have increasing demand in the world market. It is very good attempt to establish herbal gel of guava leaf extract with turmeric rhizome extract. The data presented in this study, it was demonstrated that the developed herbal gel formulation F(mixed) possess significant, therapeutically efficacious, suitable vehicle for drug delivery in low cost but definitely with high potential. The result showed that due to combination dosage form developed new herbal gel formulation having good antifungal activity as well as anti-inflammatory activity so it is safe, stable and good for mouth ulcer treatment.

REFERENCES

1. Singh M et al, Formulation and Evaluation of Herbal Gel Containing Ethanolic Extract of *Ipomoea Fistulosa*, *International Journal of Science and Research*, 2014, 3(7), 1862-1866.
2. www.healthline.com
3. Joy P ,Thomas J ,Mathew Samuel, Skaria Baby P. Medicinal plants, Kerala agricultural University: Aromatic & medicinal plants Research Station ; 1998 P:1-211
4. Thomas J, Medicinal & aromatic plants research in India. In UNDP, process training course on Indigenous medicinal & aromatic plants, Beijing, China; 1997,17-27.
5. Mital Kaneria, Sumitra chanda, Phytochemical and Pharmacognostic Evaluation of leaves of *Psidium Guajava* L. (Myrtaceae), *Pharmacognosy Journal*, 2011, 3(23), 41-45.
6. Preeti Rathaur, Waseem Raja, P.W. Ramteke and Suchit A. John. Turmeric: The golden spice of life. *International Journal of pharmaceutical sciences and research*.2012;3(7):1987-1994
7. S´anchez E, Heredia N and Garc´ia S., Extracts of edible and medicinal plants damage membranes of *Vibrio cholerae*. *Applied and Environmental Microbiology*, (2010), 76 (20), 6888–6894.

8. Das S. et al, Formulation and evaluation of herbal gel containing Clerodendron fortuneatum leaves extract, International Journal of PharmTech Research, 2011, 1(3), 140-143.
9. Mayur Mokashi et al, Formulation and Evaluation of Herbal Gel Containing Methanolic Extract of Annonasquamosa Leaves, International Journal of Science and Research (IJSR), 2015, 1064-1065.
10. Thombre et. al., Formulation and Evaluation Pharmaceutical Aqueous Gel of Powdered Cordia Dichotoma Leaves With Guava Leaves, American Journal of PharmTech Research. 2018; 8(2), 269-274.
11. Divesh yogi et al., Formulation and evaluation of gel containing amlexanox for mouth ulcer, International Journal of Pharmaceutical research and Bio-Science, 2015; Volume 4(2): 356-364
12. Kaur LP, Garg R, Gupta GD , Development and Evaluation of Topical gel of minoxidil from different polymer bases in application of alopecia. Int. J. Pharmacy and Pharm. Sci. 2010, 2: 43-7.
13. Mendhekar et al. Formulation and evaluation of gel containing Neem, Turmeric, Aloevera, Green tea and Lemon extract with activated charcoal and honey. European Journal of Pharmaceutical and Medical Research, 2017 439-444.
14. Pandey, Formulation And Evaluation of Invitro Antimicrobial Activity of Gel Containing Essential Oils And Effect of Polymer on Their Antimicrobial Activity, International Journal of Pharmacy And Pharmaceutical Sciences, 2011, 3(1), 234-23
15. Koland M, In vitro and in vivo evaluation of chitosan buccal films of ondansetron hydrochloride, International Journal of Pharmaceutical Investigation, 2011, 1(3), 164-171.
16. Adapa Satish Kumar et al. Formulation and evaluation of an herbal mouth gel containing methanolic extract of Psidium guajava tender twigs for treating oral mucositis, J Global Trends Pharm Sci 2016; 7(1): 3009-3012
17. Japan Patel et al: Formulation And Evaluation of Topical Aceclofenac Gel Using Different Gelling Agent, International Journal of Drug Development & Research, 2011,3 (1),156-163.