Original Article

TIPS Trends in Pharmaceutical Sciences 2024: 10(1): 57-66.

Preparation and evaluation of a mastic gum Peel-off mask as a skin-refreshing product

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Abstract

As the first link in the ecological chain, plants play an important role in human life. Their application as a group of ingredients in cosmetic products is one of the most important issues in the field of specialized skin and beauty management. Among these plants, the mastic plant and the preparation, gum, with the scientific name *Pistacia lentiscus* L., (Anacardiaceae family) are interesting for producing cosmetic products. In the present study, Mastic gum has been evaluated in terms of preparation for a Peel-off gel mask as well as assessment of physicochemical and phytochemical properties. Analyses such as Gas chromatography fingerprint and infrared spectroscopy were performed, and then the gum gel sheet mask formulation was prepared. The main compound in the analysis of GC/MS results of plant essential oil was α-Pinene with 65.78%. Following the preparation of the peel-off mask, the pharmaceutical evaluations related to the product including product color and odor test (organoleptic), product stability test, pH determination, conductivity, spreadability, and microbial total count were performed. The obtained outcomes showed the appropriate characteristics of the product for topical application. It is considerable that by completing the clinical processes and fulfilling the standardization procedure of the active ingredient and formulation, this mask can be presented as a suitable candidate in the cosmetic field and available in the market.

Keywords: Cosmetics, Peel-off mask, Standardization, Mastic, Fingerprint

Please cite this article as: Ashrafi H, Havaie M, Zarshenas MM*. Preparation and evaluation of a mastic gum Peel-off mask as a skin-refreshing product. Trends in Pharmaceutical Sciences. 2024;10(1):57-66. doi: 10.30476/TIPS.2024.100890.1223

1. Introduction

Recently, cosmetics and skin care products have gained special importance in daily life and are used regularly. Cosmetic products with natural ingredients have created a new branch in the subject of cosmetic hygiene and formulation (1). These products, which are a combination of cosmetic ingredients and medicinal products, can lead to an improvement in skin function and health (2). It is very important to choose the proper product related to the patient's disease and skin problems. There are different types of skin care products (2).

One of those types is known as skin topical preparations. The advantages of topical administration include easy acceptance of the patient, wide availability of medicine, easy access, and non-invasiveness of this treatment method. The semi-solid pharmaceutical form is easy to use and useful for drug delivery of a wide range of pharmaceutical molecules Topical products have forms, one of the most used of which is the medicinal form of gel (3). Gels contain small minerals or large organic molecules suspended in a liquid (4). Gels are homogeneous semi-transparent forms with a hydrophobic or hydrophilic network structure and

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Received: 21/10/2023; Accepted: 01/03/2024

consist of a liquid phase inside a polymer matrix with physical or sometimes chemical cross-links along with gelling polymers that can be synthetic, semi-synthetic, or natural (11).

Face masks, considerably are one of the types of cosmetic products, effective in skincare that can be used manually. These masks have many applications and are classified into 4 different types sheet mask, hydrogel, rinse-off, and peel-off mask (5).

Peel off mask is one of the latest types of masks formulated for the beauty and improvement of facial skin complications. The advantages of these masks have made them to be at the top of people's needs. Peel-off masks act by penetrating deep into the skin pores and removing dead cells along with impurities and pollution in the outermost layer of the skin. Peel-off masks increase skin water by blocking skin pores (6).

Regarding the desire of consumers to use natural resources, more safety, fewer side effects, better compatibility and variety, and the fair price and long-term effectiveness of herbal masks, the use of industrial herbal masks has flourished (6). Characteristics such as stability, pH determination, spreadability, viscosity, color, smell, and organoleptic characteristics (7, 8) are the factors that a facial mask formulation should be evaluated based on to have the ability to enter the consumer market.

In traditional Persian medicine (TPM), the use of plants in the preparation of cosmetics and skin care products has a long history. One of the plants that can be used as a candidate in cosmetic products is the Mastic plant. The mastic plant with the scientific name Pistacia lentiscus L. (Anacardiaceae) has a hot and dry nature. The therapeutic part of this plant is its gum, which is prepared from the grooves inserted into its stem and branches. Its color is pale yellow and slightly transparent, and its smell is mild and pleasant (9). The opinion of the sages of traditional medicine is that it causes the skin to shine (transparency and improvement of the appearance of the skin) (9).

With the descriptions given about face masks and considering the use of medicinal plants in these formulations, the main aim of this research is to design and formulate a peel-off mask containing mastic gum, with a topical skin-refreshing effect.

2. Material

2.1. Sample and extract preparation

Following authentication and specifying the voucher number, the desired gum sample was powdered by an electric mill to increase the contact surface of the sample with the solvent for the extractions. The resulting powder was stored in a freezer at -20 °C for pharmacognostic and pharmaceutical evaluations. In parallel, a part of the resulting powder was subjected to hydrodistillation and extraction of the essential oil.

To prepare the mastic extract, 350 ml of 70% hydro-alcoholic solution was added with 50 g of mastic powder in a one-liter flask and mixed well. In the next step, the mentioned mixture was sonicated by an ultrasonic bath at a temperature of 40 degrees Celsius for 20 minutes. Then the contents were filtered by filter paper and funnel, then the liquid was passed through the filter and collected and concentrated by a rotary device. The concentrated extract was transferred to two 50 ml flasks and completely dried by a speed vacuum machine for 24 hours.

2.2. Essential oil extraction and analysis

To prepare the essential oil and carry out the identification and standardization steps, the preparation of the essential oil by distillation with water (using a Clevenger for 4 hours) was considered. At the end of the process, the amount of essential oil extracted from the specified amount of powder was calculated. The resulting essential oil was stored in an Eppendorf and a freezer at -20°C until it was injected into the GC/MS machine to determine the profile of the essential oil. Then the essential oil was subsequently injected into the GC/MS apparatus and the final compounds were identified through mass spectrum measurement. The inhibition coefficient or KI of compounds was calculated using the following formula in equation 1:

$$KI = 100 \times \left[n + (N - n) \times \frac{t_r(Unknown) - t_r(n)}{t_r(N) - t_r(n)} \right] \quad \text{(Eq. 1)}$$

2.3. Determination of powder particle size and distribution (Powder evaluations)

Forty grams of the milled powder was evaluated with a vibrating sieve device to check

the particle size distribution. Sieves with mesh numbers 10, 20, 30, 35, 50, 60, 70, 80, 100, and 150 were placed on top of each other from the mesh with the lowest number to the highest number. The weighed powder was sieved for 10 minutes at a speed of 10 rpm. After finishing the work, the weight of the powder sample remaining on each sieve was measured (10). After calculating the cumulative percentage, its span was calculated. The weight and cumulative percentage of the remaining mass on each sieve were calculated. According to the following formula (11), the value of span was calculated for the powder obtained from each run (Equation 2).

$$Span = \left(D_{90} - D_{10}\right) / D_{50} \quad \text{(Eq. 2)}$$

2.4. Bulk density and Hausner ratio

Exactly, 28 grams of the powder sample was subjected to machine blows for 3 minutes. The primary and secondary volumes were read and reported, and the Hausner ratio was calculated (Equation 3) (12).

$$Hausner\ ratio = \left(tapped\ density\ /\ poured\ density\right) \times 100 \quad \text{(Eq. 3)}$$

2.5. Determination of the angle of repose

The angle of repose is used as an indirect method to quantify powder flow due to its relationship with interparticle cohesion (13). In this research, the fixed height funnel method was used to measure the angle of repose. First, the funnel with an end diameter of 1 cm was placed on a metal clamp 8 cm from the plate and perpendicular to it. Then, the powders were poured from the funnel onto the bottom plate. Then, the diameter of the formed circle was measured. This process was repeated three times for each powder. Finally, the angle of repose was calculated using the equation 4.

$$Tan\ \theta = \frac{2H}{D^0} \quad \text{(Eq. 4)}$$

2.6. Peel off mask preparation

First, 5 grams of mastic gum (powder and extract were investigated in this study) was added to 30 ml of ethanol (96°) in a 200 ml beaker and on a heater stirrer at 45°C. After about 25 minutes, when most of the gum powder was dissolved, half of the required amount of water was added to it, which made a mixture with good reflection in color. Then, 10 grams of polyvinyl alcohol was added to the mixture in several steps giving time to dissolve well. Then, 3 ml of glycerol and 0.5 ml of Tween 20 were added to it, and after the relative uniformity of the contents inside the beaker, it was brought to the required volume with the rest of the distilled water. Finally, the heater was turned off, and the formulation was homogenized at 2000 rpm for 15 minutes with a homogenizer (Heidolph®).

2.7. Evaluation of pharmaceutical properties of the mask

2.7.1. Organoleptic test

The color and smell of products from the same production series were compared at the end of the 1st, 2nd, 3rd, 8th, 15th, and 30th day after the product was produced (14).

2.7.2 pH evaluation

A pH meter was used to evaluate and determine the pH values. pH was measured on days 1, 2, 3, 8, 15 and 30 (14).

2.7.3 Determination of the conductivity

Conductivity was measured by glass electrodes on days 1, 2, 3, 8, 15 and 30 (14).

2.7.4. Rheological properties

The rheological properties of the gel were evaluated and reported in this test by cone and plate rheometer (Brookfield®).

2.7.5 Evaluation of spreadability

To evaluate the spreading of the mask, 0.5 grams of the product was placed under standard conditions between two glass plates under the force of 42 grams, 242 grams, and 542 grams, and the surface covered by it was measured in square millimeters after bearing the pressure for three minutes. Ideally, the surface covered by a 42-gram weight should be more than 300 square millimeters, a 242-gram weight should be more than 700 square millimeters, and a 542-gram weight should be more than 1000 square millimeters (15).

2.7.6 Homogeneity of formulation

Thirty grams of the product were added

into the tube and the end of the tube was pressed. Then, a slight pressure was applied to the product tube and the outer strip of the product was checked for uniformity and homogeneity without phase separation (14).

2.7.7 Physical stability

To control the stability of the desired formulation, it was kept at -4°C for four weeks. Comparing with samples at room temperature, their physical reversibility and possible changes were checked every week.

The amount of 5 to 10 grams of the final formulation was transferred into the falcon tube and the stability test of the gel was performed by a centrifuge model Z200A at a speed of 3000 rpm and the possible separation of phases was investigated at different times between 5 and 30 minutes.

2.8. Total microbial count

All the necessary tools and containers were autoclaved before starting each step of the work. The final formulation sample was prepared following Iran's drug and food standards and finally, it was evaluated for microbial evaluation in the microbial control laboratory to check for the presence of microorganisms. These tests include determining the total number of microbes, which in this pharmaceutical form should not be more than 100 non-pathogenic masses per gram. Determining the total number of molds and yeasts in this pharmaceutical form should not be more than 100 mass per gram. It was also checked for the absence of Staphylococcus aureus, Pseudomonas aeruginosa, and Escherichia coli in this pharmaceutical form.

2.9. Statistical analysis

All data were statistically analyzed with Microsoft Excel, 2016.

3. Results and Discussion

3.1. Yield of extraction

The extraction yield was calculated as 13.97% W/W.

3.2. Yield of the essential oil extraction

The result related to the essential oil extraction yield of the Mastic sample was calculated at 0.6 % (W/W).

3.3. Gas chromatography/ Mass spectroscopy and data analysis

One microliter of the essential oil sample was injected into the GC/MS. The results of the GC/MS analysis are given below. The most significant compound in essential oil, α-Pinene, was identified with 65.78% abundance (Table 1).

3.4. Determination of powder particle size and distribution (Powder evaluation)

Span of the powder was calculated as 0.96.

3.5. Bulk density and Hausner ratio

Following the determination of the primary volume equal to 55 and the secondary volume equal to 38 ml, Hausner's ratio was calculated equal to 1.44.

3.6. Determination of the angle of repose

After the final powder was slowly added from the funnel onto the bottom plate, the diameter and height of the formed cone were measured and the angle of repose was calculated as 42°.

3.7. Peel-off gel mask preparation

To prepare the Peel gel mask formulation from Mastic, various parameters including gelling

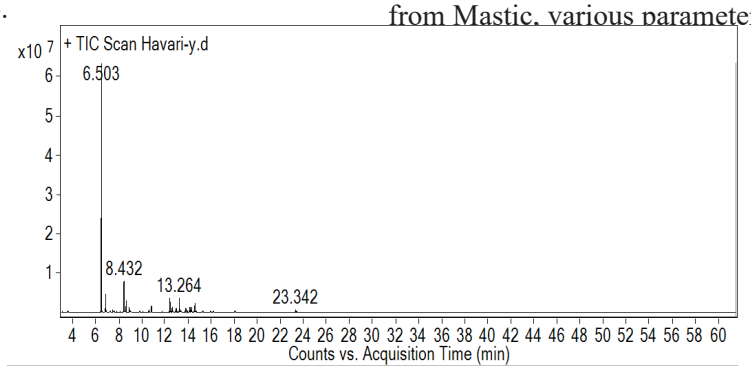

Figure 1. The chromatogram of Mastic essential oil

Table 1. Essential oil constituents of mastic gum.

No.	Component	RT (min)	Prevalence (%)	RICal.	RIRef.
1	α-Pinene	6.5	65.78	932.681	932
2	Camphene	6.8	2.98	946.458	945
3	α-Terpinene	8.4	6.5	1006.250	1006
4	Cymene	8.6	2.48	1011.902	1009
5	α-Dimethyl styrene	10.6	0.56	1071.501	1073
6	α-Terpinolene	10.8	1.36	1077.691	1077
7	Pinocarveol	12.4	3.74	1122.344	1121
8	3-Pinanone	12.9	1.3	1135.729	1134
9	Myrtenal	14.1	1.42	1166.953	1168
10	Terpineol	14.2	1.46	1170.234	1170
11	Verbenone	14.5	3.18	1178.932	1183
	Identification (%)		90.76		

agent, co-solvent, surfactant, and emulsifier were tested and evaluated until finally a formulation with ideal properties was prepared.

3.8. Selection better gelling agent

Polyvinyl alcohol polymer with a molecular weight of 72000 was selected as the gelling agent in this research (Table 2).

3.9. Determination of the amount of polyvinyl alcohol polymer

According to the obtained results, when 10% of the polymer was used in the formulation, the characteristics of uniform spreading on the skin and other properties of the product were more suitable compared to other percentages. Accordingly, the amount of polymer in the formulation was determined as 10%.

3.10. Determination of the proper percentage of the co-solvent

The formulation was selected with the help of 40% solvent and the homogenizing agent was added to it to check the presence of the solvent and the homogenizing agent together.

3.11. Determination of the presence of emulsifier in the formulation

The formulation containing 40% ethanol and 3% glycerol created a softer and better feeling on the skin and was smoother, and compared to the formulations containing propylene glycol, it was separated from the skin in one piece and smoother. By checking the pH of the product and considering the acidity of the skin's pH, the formulation containing Tween 20 was selected for the final formulation.

3.12. The final peal-off mask formulation with mastic powder and extract

The mastic powder with different percentages was added to the formulation, and due to the spreadability and homogenous texture of the formulation, the 5% (w/w) of powder was selected. Subsequently, different percentages of mastic extract were also evaluated in the formulation and the formulation with 5% (w/w) extract was selected based on its spreadability and homogenous texture.

The Peel-off mastic gum powder mask

Table 2. Selective gelling agents.

Formulation	Polymer type	Result
1	Polyvinyl alcohol 24000	Low viscosity and consistency and inappropriate spreadability
2	Polyvinyl alcohol 72000	More appropriate viscosity, consistency, and spreadability than formulation 1
3	Polyvinyl alcohol 145000	High viscosity and consistency, poor spreadability, with a time-consuming dissolution process

Table 3. Mask formulation components (Mastic powder and extract).

Constituents	% in Formulation	% in Formulation
Polyvinyl alcohol 72000	10	10
Ethanol 96	40	40
Glycerol	3	3
Tween 20	0.5	0.5
Mastic powder	2 and 5	
Mastic extract		2 and 5
Water	Up to 100 ml	Up to 100 ml

formulation with the mentioned components was selected as the final formulation, and pharmaceutics evaluations were carried out on it. The peel-off mask formulation of Mastic extract with the components mentioned in the table was selected as the final formulation, and pharmaceutics evaluations were done on it (Table 3).

3.13. Evaluation of pharmaceutical properties of the mask

3.13.1. Organoleptic test

The color and smell of formulations from the same production series at the end of specific periods (end of day 1, 2, 3, 8, 15, and then the first month) were compared after the production of the product, and no change in color and smell was seen in any of the products.

3.13.2. pH evaluation

pH measurement was done on days 1, 2, 3, 8, and 15, then the first month, and the corresponding results are given in the table 4.

3.13.3. Determination of the conductivity

The electric conductivity of the formulations was measured by glass electrodes, and the relevant results can be seen in Table 5.

3.13.4. Rheological properties

The rheological profiles of the gel were evaluated by the rheometer device using the cone and plate method, the results of which can be seen in the figure below (Figures 2 to 4)..

3.13.5. Evaluation of spreadability

The spreadability of the formulations was measured under standard conditions by two glass plates under different forces, and the results can be seen in the table 6.

Table 4. Stability results of pH measurement in powder and extract.

		pH values					
Product	Mastic content	Day 1	Day 2	Day 3	Day 8	Day 15	pH (Month 1)
1	Powder 5%	5.11	5.54	5.65	5.51	5.43	6.15
2	Extract 5%	4.74	4.73	4.63	4.67	4.69	4.54

3.13.6. Physical stability

In products containing mastic gum powder, a very small amount of powder deposition was seen on the bottom of the container. However, in the products containing mastic gum extract, no changes were observed compared to the original products.

3.13.7.Gel stability test

The possible separation of phases was investigated at different times (between five minutes and half an hour) after centrifugation of the gel at a speed of 3000 rpm. This did not happen and their

Table 5. The results of determining the electric conductivity (in millivolts).

		Electric conductivity (in millivolts)					
Product	Mastic content	Day 1	Day 2	Day 3	Day 8	Day 15	pH (Month 1)
1	Powder 5%	53.10	68.20	70.30	75.10	78.00	121.00
2	Extract 5%	113.00	110.10	113.00	117.20	119.00	123.80

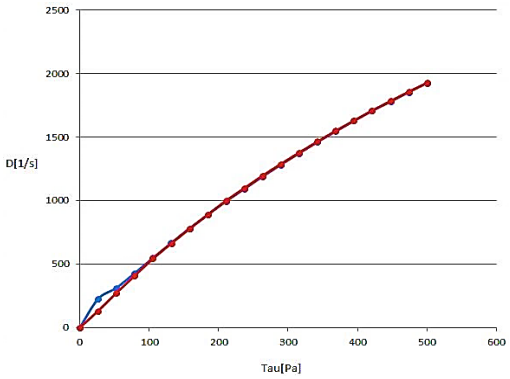

Figure 2. The rheology of the formulation (without powder): The red line is return chart; Blue is The chart went.

stability was maintained.

3.13.8. Total microbial count

The results of the total microbial count of the final formulation sample are given in the table 7.

4. Conclusion

Today, natural compounds and medicinal plants, as a group of compounds in cosmetics, are among the most important items in the discussion of specialized skin and beauty treatments. This issue is mainly due to the evidence of side effects and the tendency to use natural products as much as possible in order to maintain health. Also, complications of the modern pharmaceutical system, such as high costs, the use of non-renewable resources such as fossil resources, environmental pollution, and the inability to prepare or to synthesize pure phytoactive compounds, cause more attention to the medicinal plant. The traditional use of plants to treat skin diseases and problems, as well as maintain beauty, freshness, and health has been widespread (1).

Recently, the use of homemade masks has increased due to reasons such as fewer side effects, greater compatibility with skin types, safety and variety, more reasonable prices, and the desire of consumers to use natural resources (1, 16). On the other hand, Peel-off masks have been developed by the pharmaceutical industry due to their ease of use by consumers and other advantages (17, 18).

Therefore, in the present study, mastic gum has been evaluated in terms of preparation as a Peel-off mask, as well as the investigation of physicochemical and phytochemical properties. Among these evaluations, gas chromatography fingerprints with a mass spectrometer and infrared spectroscopy were considered as primary controls of the starting material. The GC/MS spectrum can help in the analysis of these volatile compounds,

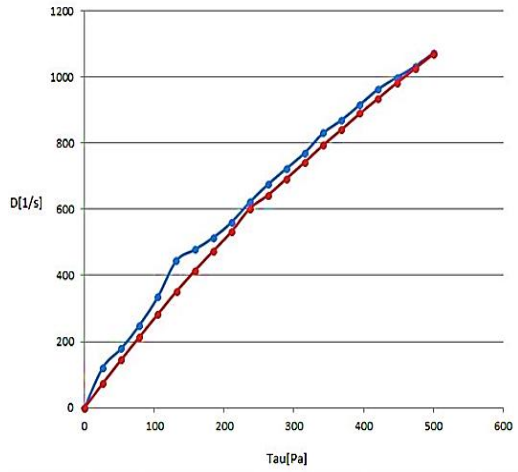

Figure 3. The rheology of the formulation (with powder): Red line is return chart; Blue is The chart went.

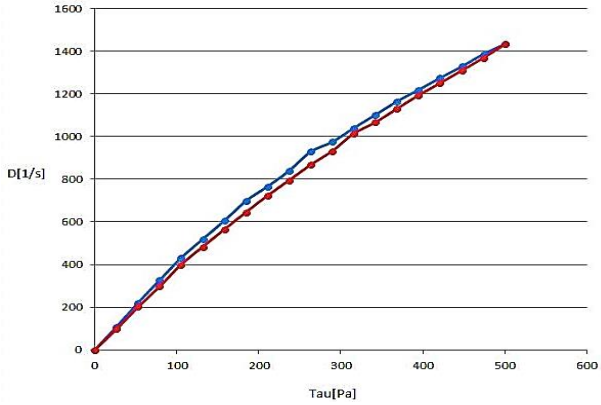

Figure 4. The rheology of the formulation (with extract): Red line is return chart; Blue is The chart went.

formulation, standardization, and as a fingerprint in the identification and standardization of mastic masks (19). The main volatile compound in mastic was reported as α-Pinene with 65.78%.

In the next step, the angle of repose and Hausner ratio were used to evaluate the properties of the powder. The angle of repose of the final powder was measured as 42, which is placed in the "passable" category (7). The compressibility index of the final powder was measured as 1.44. This type of powder was placed in the category of powder with poor flowability (7).

In the next step, the preparation of the Mastic peel-off mask formulation was carried out. In the peel-off mask, 10% polyvinyl alcohol 72000 due to appropriate viscosity and spreadability (as a gelling agent) (20), 40% ethanol 96% due to high evaporation rate, polyvinyl alcohol polymer, and hydroalcoholic extract (21, 22), 3% glycerol due to the uniform separation of the gel and causing less side effects on the skin (22), and 50.0% of Tween 20 (as a surfactant) (23) were mixed. Due to the pleasant smell of the final formulation, odor-masking excipients were not used in the formulation. Mastic powder was used in the amount of 5%.

Quality control tests include organoleptic and physical tests (such as color and odor tests, gel stability and durability, pH determination, electric current conductivity determination, consistency, spreadability, and homogenous release), and microbiology tests on the formulations were included with positive results (24). At the end of the determined times, no change in the color and smell of the examined samples was observed. The product did not contain any of the examined microorganisms. Performing the centrifuge process is, in most cases, an estimated quality index for the separation of different phases of semi-solids (24). On the other side, the fluidity and rheological properties of the gels were evaluated by the cone and plate rheometer.The rheological behavior of the obtained formulation has shown low thixotropy and pseudo-plastic characteristics, especially when mastic extract or powder is in the formulation, these characteristics can be seen more.

The normal pH of the skin is in the range of 5.4-5.9. Therefore, natural skin has weak acid properties. The growth and proliferation of microbes on the skin are limited due to its acidic properties. Therefore, products that increase the pH of the skin provide the basis for microbial growth (25). Herein, the final product with an acidic pH can be suitable. In the study, no significant changes were observed in pH value.

The results related to the study of electrical conductivity for selected formulations showed no significant changes during the evaluation pe-

Table 6. Results of the extensibility and spreadability test.

Formulation	Area in mm2 (42 g pressure)	Area in mm2 (200+42 g pressure)	Area in mm2 (500+42 g pressure)	Area in mm2 (1000+42 g pressure)
Powder	961.63	1256.00	1962.50	3846.50
Extract	961.63	1256.00	1808.64	3316.63

Table 7. Total microbial count in the final formulation.

Test title	Outcome	Reference
Total bacterial count/g	< 100 CFU	< 105 CFU
Mold and yeast/g	< 100 CFU	< 103 CFU
Pseudomonas aeruginosa/g	Negative	Negative
Escherichia coli/g	Negative	Negative
Staphylococcus aureus/g	Negative	Negative

riod. In the evaluation of the spreadability of the desired gels, the spreadability after placing the weight of 42 g was more than 300 square millimeters, for the weight of 242 g, it was more than 700 square millimeters, and for the weight of 542 g, it was more than 1000 square millimeters, so the results obtained are within the permissible range mentioned in the references (26) and according to the same study, it indicates that when a person uses a certain dose of the product, it spreads easily on the skin and has a uniform distribution (24). In the homogeneity test of the gels, the formulations were removed from the tube in a continuous flow and by applying slight pressure.

According to the documentation available in traditional Persian and modern medicine on the properties of mastic gum, this study aimed to formulate a peel-off gel mask of mastic gum and to evaluate the physicochemical evaluations. In general, the observations obtained from the physicochemical evaluation tests of the formulations have all had favorable results and show that the said formulations can be used as effective cosmetic products in the health and beauty of the skin after obtaining a license from the Deputy Food and Drug Administration. to be presented to the herbal medicinal market of Iran.

Acknowledgment

The authors of this manuscript wish to express their thanks to Shiraz University of Medical Sciences, Shiraz, Iran (Project No: 25787).

Conflict of Interest

The authors declare no conflict of interest.

References

1. Pieroni A, Quave CL, Villanelli ML, Mangino P, Sabbatini G, Santini L, et al. Ethnopharmacognostic survey on the natural ingredients used in folk cosmetics, cosmeceuticals and remedies for healing skin diseases in the inland Marches, Central-Eastern Italy. *J Ethnopharmacol*. 2004 Apr;91(2-3):331-44. doi: 10.1016/j.jep.2004.01.015. PMID: 15120458.
2. Saha R. Cosmeceuticals and herbal drugs: practical uses. *Int J Pharm Sci Res*. 2012;3(1):59-65.
3. Gupta P, Garg S. Semisolid dosage forms for dermatological application. *Pharm Technol.* 2002;26:144-62.
4. Merad M, Manz MG, Karsunky H, Wagers A, Peters W, Charo I, Weissman IL, Cyster JG, Engleman EG. Langerhans cells renew in the skin throughout life under steady-state conditions. *Nat Immunol.* 2002 Dec;3(12):1135-41. doi: 10.1038/ni852. Epub 2002 Nov 4. Erratum in: Nat Immunol 2003 Jan;4(1):92. PMID: 12415265; PMCID: PMC4727838.
5. Sharma B, Singh LR, Pradesh U, Pradesh U. Pharmaceutical gels for topical drug delivery: An overview. *Int J Pharm Sci Res.* 2018;3(2):19-24.
6. Nilforoushzadeh MA, Amirkhani MA, Zarrintaj P, Salehi Moghaddam A, Mehrabi T, Alavi S, Mollapour Sisakht M. Skin care and rejuvenation by cosmeceutical facial mask. *J Cosmet Dermatol.* 2018 Oct;17(5):693-702. doi: 10.1111/jocd.12730. Epub 2018 Aug 21. PMID: 30133135.
7. Salmannejad F, Qorab H, Ghari T. Formulation, characterization and optimization of peel-off gel of soybean extract as a face mask. *Trop J Nat Prod Res.* 2024 Jun 5;8(3):6544-51.
8. Nemati MM, Abedi M, Ghasemi Y, Ashrafi H, Haghdel M. Formulation and evaluation of antioxidant and antibacterial activity of a peel-off facial masks moisturizer containing curcumin and Rosa Damascena extract. *J Cosmet Dermatol.* 2024 Feb 26.
9. Mak S. Makhzan ol Advieh. Tehran, Intis-

harat va Amoozesh enghelab Islami Press (Lithograph in Persian). 1992;PP 742-743.
10. Buanz A. Powder characterization. Remington: Elsevier; 2021. p. 295-305.
11. Saw HY, Davies CE, Paterson AH, Jones JR. The influence of particle size distribution and tapping on the bulk density of milled lactose powders. In: Chemeca 2013: Challenging Tomorrow 2013 Jan 1 (pp. 299-303). Barton, ACT: Engineers Australia.
12. Altino HO, Lourenço GA, Ataíde CH. System development for bulk density data acquisition of granular materials: Effect of operational conditions and optimization. *Powder Technol*. 2021 Oct 1;391:184-97.
13. Al-Hashemi HMB, Al-Amoudi OSB. A review on the angle of repose of granular materials. *Powder technol.* 2018;330:397-417.
14. Patel H, Panchal MS, Shah S, Vadalia KR. Formulation and evaluation of transdermal gel of sildenafil citrate. *Int J Pharm Res Allied Sci.* 2012 Mar 5;1(3):103-8.
15. Inoue Y, Suzuki K, Maeda R, Shimura A, Murata I, Kanamoto I. Evaluation of formulation properties and skin penetration in the same additive-containing formulation. *Results Pharma Sci.* 2014 Sep 23;4:42-9. doi: 10.1016/j.rinphs.2014.09.003. PMID: 25756006; PMCID: PMC4348512.
16. Joshi LS, Pawar HA. Herbal cosmetics and cosmeceuticals: An overview. *Nat Prod Chem Res*. 2015;3(2):170.
17. Sonika P, Akanksha S, Rajesh T, Sunita S, Suman S. Development and evaluation of antimicrobial herbal cosmetic preparation. *Afr J Pharm Pharmacol.* 2014;8(20):514-28.
18. McKennon SA, Schauerhamer MB, Fudin HR, Babin JL, Shane-McWhorter L. Assessing pharmacy student confidence to answer patient questions regarding herbal medicines and natural product drugs. *Curr Pharm Teach Learn*. 2018 May;10(5):643-650. doi: 10.1016/j.cptl.2018.02.005. Epub 2018 Feb 24. PMID: 29986825.
19. Ekka NR, Namdeo KP, Samal PK. Standardization strategies for herbal drugs-An overview. *Res J Pharm Technol*. 2008;1(4):310-2.
20. Çavuş S, Durgun E. Poly (vinyl alcohol) based polymer gel electrolytes: investigation on their conductivity and characterization. *Acta Phys Pol A*. 2016;129(4):621-4.
21. Elia V, Marchettini N, Napoli E, Niccoli M. The role of ethanol in extremely diluted solutions: Calorimetric and conductometric measurements. *J Therm Anal Calorim*. 2014;116:477-83.
22. Ren X, Wang C, Zhou B, Fang H, Hu J, Zhou R. Ethanol promotes dewetting transition at low concentrations. *Soft Matter*. 2013;9(18):4655-60.
23. Kothekar SC, Ware AM, Waghmare JT, Momin SA. Comparative analysis of the properties of Tween-20, Tween-60, Tween-80, Arlacel-60, and Arlacel-80. *J Dispers Sci Technol.* 2007;28(3):477-84.
24. Garti N, Magdasi S, Rubinstein A. A new method for stability determination of semi-solid emulsions, using conductivity measurements. *Colloids Surf*. 1981 Nov 1;3(3):221-31.
25. Biju SS, Ahuja A, Khar RK, Chaudhry R. Formulation and evaluation of an effective pH balanced topical antimicrobial product containing tea tree oil. *Die Pharmazie-An Inter J Pharma Sci.* 2005 Mar 1;60(3):208-11.
26. Cooper MA. Optical biosensors in drug discovery. *Nat Rev Drug Discov.* 2002 Jul;1(7):515-28. doi: 10.1038/nrd838. PMID: 12120258.