FORMULATION AND EVALUATION OF MEDICATED LIP BALM CONTAINING KETOCONAZOLE FOR TREATMENT OF EXFOLIATIVE CHEILITIS

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ABSTRACT

Lip balms are formulations applied onto the lips to prevent drying and protect against adverse environmental factors. Organic lip balms nourish the lips and help to get hydrated and protect lips affected by chapping and dryness. They help to protect the natural health and beauty of the lips. Lip balms are not gender specific products and both men and women can use them. This research work focuses on the incorporation of natural waxes, sweetener, olive oil and colourant along with Ketoconazole for the treatment of a lip condition called Exfoliative cheilitis. The causative agent of this disease can be bacteria or fungus and other underlying causes also give rise to this condition.

This formulation can help to keep lips hydrated and also nourished. Prepared lip balm was evaluated for organoleptic characteristics, melting point, spreadability, pH measurement, antimicrobial study, in-vitro diffusion and stability studies. After performing stability studies at room temperature (25.0 ± 3.0 ºC), refrigeration (4± 2.0 ºC) and oven temperature (40.0 ± 2.0 ºC) for 90 days. It was concluded that prepared lip balm shows uniform nature, perfect application, without any deformation at room temperature (25.0 ± 3.0 ºC) and at refrigeration (4± 2.0 ºC). Organic lip balm can be a better option for treatment of various lip problems.

KEYWORDS: Ketoconazole, Exfoliative cheilitis, organic, lip balm, natural.

INTRODUCTION

Lips are the most susceptible to dryness and cracking than any part of the skin. Topical lip balm products protect and help restore lips from the effect of dryness and cracking. Lip balms are formulations applied onto the lips to prevent drying and protect against adverse
environmental factors. Numerous lip balms of chemical origin are currently available in the market from companies like the body shop, Nivea, Himalaya, etc.\(^1,2\) The cosmetic literature reports on lip balm are limited, and data linked to lipstick are applicable to lip balm, because it is a cosmetic form similar to lip balm. The evaluation parameters like organoleptic, pH and stability requirements such as resistance to temperature variations, pleasant taste, smoothness during application, adherence and easy removal are also similar for both lip balm and lipstick. Lip balm should not be compared to lip gloss, with the former is a product intended for both men and women.

To formulate lip balms, it is necessary to balance the concentration of the main ingredients including butters, oils and waxes and other excipients. Many people seek weekly facials, daily skin scrubs, anti-aging lotions, and many other products to ensure they have healthy and glowing skin. But with all the attention being given to healthy skin, lip care is largely forgotten. Natural lip balms offer a natural way to maintain and promote healthy lips. Lip balms are often eaten away by the user and hence it is imperative that health regulators have a microscopic look at the ingredients that go in to the lip balm. The dyes that contribute to the color of the lip balm are dangerous to humans on consumption. Hence, natural lip balm are preferred.\(^1,2,3\)

**Advantages of natural lip balm\(^2,3\)**

i. Lip balms help to protect the natural health and beauty of the lips.

ii. Lip balms are proved to prevent ultraviolet rays from hurting the lips.

iii. They are not gender specific products and both men and women can use them.

iv. Lip balm products help to protect lips affected by cold sores, chapping and dryness.

v. Lip balm forms a homogeneous layer over the lips in order to protect the labial mucous susceptible from environmental factors such as UV radiation, dryness and pollution.

vi. It refreshes, renews and prevents lip-related symptoms resulting from colds, flu and allergies.

**Disadvantages of natural lip balm\(^3,4\)**

i. Lip balms made of low-quality ingredients can harm the lips. Such lip balms may cause drying of lips instead of moisturizing.

ii. Lip balm addiction is another disadvantage usually seen with the use of them.

iii. Compared to commercially-prepared lip balms, homemade lip balms tend to stay on the lips for a shorter duration of time. Thus, need to reapply often.
iv. Some companies manufacture lip balms considering only the beauty aspect, ignoring the health benefits and soft character of the skin. Such products will gradually damage the natural color, softness and glow of the lips.

vi. The naturally derived colors and flavours are more difficult to obtain and also have issues related to stability in the products.

vii. Natural oils have other disadvantages such as greasiness, comedogenic, and less spreadability.

Exfoliative cheilitis\textsuperscript{[3,4,5,6]}

Exfoliative cheilitis is a rare reactive condition presenting as continuous peeling of the lips. Factitial cheilitis can appear as exfoliative cheilitis when it is due to attention-seeking or factitial behaviour or an obsessive-compulsive tendency to pick or chap the lips (exfoliative). It affects both sexes equally and mainly affects young adults less than 30 years of age. Some patients diagnosed with Exfoliative cheilitis actually have a localized form of psoriasis.

The underlying causes of exfoliative cheilitis can be made worse by mouth breathing, lip licking, lip sucking, lip picking, lip biting, bacterial (Staphylococcus aureus) or yeast infection (Candida albicans). Excessive keratin formation results in abnormal peeling.

Clinical features of exfoliative cheilitis\textsuperscript{[3,4,5]}

Exfoliative cheilitis presents with continuous peeling of the vermilion (outer) part of the lips. It may affect just one lip, usually the lower. The lip may look normal or red before the formation of the thickened surface layer. The peeling appears to be cyclical and proceeds at different rates in different sites, so there is always some part of the lip peeling at any time. There may be associated bleeding resulting in the formation of a hemorrhagic crust. When both lips are involved, the lower lip is usually more affected than the upper. The condition may be painful, causing difficulty in eating and speaking. Other symptoms reported include sensations of tingling, itching, ulceration or fissuring and dryness. Diagnosis can be done by
swabs for candida and Staphylococcus aureus infection and biopsy should be done but histopathology may be nonspecific.

MATERIALS AND METHODS
The drug Ketoconazole was purchased from Yarrow Chem products, Mumbai. The waxes i.e, candelila wax, bees wax and cocoa butter were purchased from Research lab fine chem industries, Mumbai. Stevia powder, olive oil and beetroot powder were purchased from a local supermarket.

Formulation of Lip Balm-

a. Weigh all the ingredients.
b. Melt the weighed amount of waxes in an electric water bath in descending order of their melting point.
c. First add candelila wax, then beeswax and finally cocoa butter.
d. Stir continuously till the waxes melt completely.
e. Simultaneously, make a mixture of beetroot powder in olive oil.
f. Keep on a double boiler so that the colour gets blended into the oil.
g. When the desired colour intensity is reached remove the oil from boiler and strain to discard the beet powder particles.
h. Then add stevia powder which acts as a sweetener in the lip balm.
i. Vortex until the stevia powder mixes well with oil. (Note- Stevia powder remains suspended in oil and when mixed with the melted waxes remains suspended in the lip balm).
j. Add this mixture of olive oil to the melted waxes.
k. Add ketoconazole and mix to get a homogenous lip balm.
l. Pour into the clean container while still hot and allow to cool at room temperature.

Composition of lip balm is given in Table no.1.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Quantity</th>
<th>Purpose of the ingredient in lip balm</th>
</tr>
</thead>
</table>

Table no.1: Formulation table for lip balm.
<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoconazole</td>
<td>200mg</td>
<td>Antifungal drug</td>
</tr>
<tr>
<td>Candelila wax</td>
<td>0.76g</td>
<td>Hard wax which gives the desired thickness to the lip balm</td>
</tr>
<tr>
<td>Beeswax</td>
<td>1.6g</td>
<td>Good emollient action, thickener</td>
</tr>
<tr>
<td>Cocoa butter</td>
<td>2.26g</td>
<td>Imparts softness to lip balm, contains antioxidants, nourishes and moisturizes lips</td>
</tr>
<tr>
<td>Olive oil</td>
<td>5ml</td>
<td>Solvent for colourant, natural permeation enhancer, gives glossy look to lip balm</td>
</tr>
<tr>
<td>Stevia powder</td>
<td>0.3gm</td>
<td>Natural sweetener</td>
</tr>
<tr>
<td>Beetroot powder</td>
<td>0.5g</td>
<td>Colouring agent</td>
</tr>
</tbody>
</table>

![Fig. no. 1: Lip balm formulation containing Ketoconazole.](image)

**EVALUATION OF LIP BALM**

i. Melting point-
A small quantity of lip balm was filled into a glass capillary tube. One end was sealed using bunsen burner. The capillary tube was then dipped into a thiel’s tube containing liquid paraffin. The temperature range at which the lip balm melts was noted.

ii. Organoleptic properties-
The organoleptic characters such as colour, odour, taste and appearance of the lip balm were observed.

iii. Test for spreadability-
This test was done by applying lip balm on a glass slide. This test is done at room temperature and used to analyze the strength, grittiness and uniformity in colour distribution of the formulated lip balm i.e., to study whether the lip balm breaks or cracks during application. Criteria for analysis of spreadability is as follows:-

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Character</th>
</tr>
</thead>
</table>

**Table no. 2: Criteria for analysis of spreadability.**
iv. pH measurement-
The study of pH is essential as highly acidic or alkaline pH may cause irritation when the lip balm is applied. 1gm of lip balm was dissolved into 100ml of water and pH meter was used for this purpose.

v. Antimicrobial activity using filter paper method-
Candida albicans was used for the study. Potato dextrose agar was prepared, sterilized using autoclave and then poured into sterile petri plates. After cooling and solidification of the agar medium, a swab of the candida species was wiped on the entire surface of the agar. A filter paper disc of size 0.5mm was covered with the formulated lip balm on both sides and then placed at the centre of the agar plate. This petri dish was labelled as ‘test’. Another petri dish was prepared for the standard i.e. 2% Ketoconazole cream using the same procedure as mentioned for test sample. It was labelled as ‘Standard’. The petri plates were kept for incubation in incubator at 30°C for 48 hours. The zone of inhibition obtained for both the test and standard were measured and compared to know the effectiveness of the formulated lip balm in inhibiting the growth of C. albicans.

vi. In-vitro diffusion study-
In-vitro permeation studies were carried out using Franz diffusion cell with a receptor compartment capacity of 20 ml. Egg membrane was isolated and mounted between the donor and receptor compartment of the diffusion cell. The formulated lip balm was placed over the egg membrane. The receptor compartment of the diffusion cell was filled with a phosphate buffer of pH 7.4. The whole assembly was placed on a magnetic stirrer. The solution in the receptor compartment was stirred continuously using a magnetic bead at 50 rpm, with the temperature maintained at 37 ± 0.5°C. The samples were withdrawn at different time intervals and analyzed for drug content using a UV–visible spectrophotometer at 243nm. The receptor phase was replenished with an equal volume of the same medium after withdrawal.

vii. Stability studies-
Stability means how long a product can maintain its original form without any visible changes under the influence of various environmental factors like temperature, humidity and light. Stability study is necessary to determine the shelf life of the formulated lip balm.\[5,6,7\]

This was done at different temperature and humidity conditions:
Room temperature (25.0 ± 3.0 °C), refrigeration (4± 2.0 °C) and oven temperature (40.0 ± 2.0 °C) for 30 days.

RESULT AND DISCUSSION
i. Melting point- The melting point was found to be in the range 72\(^0\)-74\(^0\)C.
ii. Organoleptic characteristics- The results of organoleptic analysis were as listed in table no. 3.

### Table no. 3: Organoleptic characteristics of lip balm.

<table>
<thead>
<tr>
<th>Evaluation parameter</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>Red colour</td>
</tr>
<tr>
<td>Odour</td>
<td>No pungent odour</td>
</tr>
<tr>
<td>Taste</td>
<td>No unpleasant taste</td>
</tr>
<tr>
<td>Appearance</td>
<td>Uniform with no fragments or crystallization</td>
</tr>
<tr>
<td>Texture</td>
<td>Smooth</td>
</tr>
<tr>
<td>Greasiness</td>
<td>No greasiness</td>
</tr>
</tbody>
</table>

iii. Test of spreadability-
The formulated lip balm was found to have the features as given under criteria ‘G’ i.e., Good (uniform, no fragmentation; perfect application, without deformation of the lip balm).

iv. pH measurement-

pH of lip balm was near to neutral pH i.e. 7.2 this would not cause any irritation to lips.

v. Antimicrobial activity using filter paper method-

Zone of inhibition was observed for both test and standard sample. The diameter was measured to be 2.5cm for lip balm containing Ketoconazole as compared with the zone obtained from Ketoconazole cream which showed a diameter of 2.8cm.

vi. *In-vitro* diffusion study-
The maximum release of drug from the lip balm was found to be about 85.32% at the end of 60min.

### Table no. 4: In-vitro drug release study of lip balm.
<table>
<thead>
<tr>
<th>Time (min)</th>
<th>% Drug release</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>43.56</td>
</tr>
<tr>
<td>20</td>
<td>55.71</td>
</tr>
<tr>
<td>30</td>
<td>62.34</td>
</tr>
<tr>
<td>40</td>
<td>70.66</td>
</tr>
<tr>
<td>50</td>
<td>76.54</td>
</tr>
<tr>
<td>60</td>
<td>85.32</td>
</tr>
</tbody>
</table>

vii. Stability studies-
At the end of 30 days, the lip balm was subjected to evaluation parameters i.e., organoleptic properties, melting point, spreadability and pH. The results of stability study were observed to be as given in table no. 5.

Table no. 5: Results of stability study for 30 days.

<table>
<thead>
<tr>
<th>Evaluation parameter</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting point</td>
<td>72º-74ºC</td>
</tr>
<tr>
<td>Colour</td>
<td>Red colour</td>
</tr>
<tr>
<td>Odour</td>
<td>No pungent odour</td>
</tr>
<tr>
<td>Taste</td>
<td>No unpleasant taste</td>
</tr>
<tr>
<td>Appearance</td>
<td>Uniform with no fragments or crystallization</td>
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<tr>
<td>Texture</td>
<td>Smooth</td>
</tr>
<tr>
<td>Greasiness</td>
<td>No greasiness</td>
</tr>
</tbody>
</table>
| Test of spreadability| a. Good- uniform, no fragmentation; perfect application, without deformation of the lip balm [Room temperature and refrigeration]  
b. Intermediate- Uniform; leaves few fragments; appropriate application; little deformation of the lip balm [Oven temperature] |
| pH                   | 7.2                                                                         |
| *In-vitro* diffusion study | 82.67% drug release                                                   |

CONCLUSION
Joy et al.

Prepared lip balm formulation was evaluated for organoleptic characteristics, melting point, spreadability, pH and stability studies. This lip balm can be used as treatment measure for Exfoliative cheilitis that is diagnosed to be caused due to Candida species. Irrespective of the sex of the patient this lip balm can be used by both male and female patients. Also, it contains olive oil and cocoa butter that help to rejuvenate the lip structure by moisturizing and preventing drying of lips. The polyphenols present in olive oil have antioxidant, anti-inflammatory and antimicrobial activity. The phenolic compounds that are mainly responsible for antioxidant activity are hydroxytyrosol, tyrosol and oleuropein. Olive oil also acts as a natural permeation enhancer. The stability of the formulated lip balm was found to be good at room temperature and refrigeration, but oven temperature is not recommended. The antimicrobial study showed that the formulated lip balm is somewhat effective in preventing the fungal growth as compared to standard. Thus, it can be concluded that organic medicated lip balm can be preferred for treatment of lip diseases too.

By changing the concentration of olive oil and waxes further study can be performed to enhance the usefulness and applicability of lip balm formulation.

ACKNOWLEDGEMENTS

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REFERENCES