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Formulation And Evaluation Of Chamomile Microspheres Loaded Cream For Enhanced Topical Delivery In Acne Treatment

Rutika Rane[1*], Neha Rai[2], Archana Rajbhar[3], Kirti Raut[4], Rajnish Rai[5]

Ms. Suvarna Patil[6]

[1,2,3,4,5] Research Scholar, Ideal College of Pharmacy and Research, Kalyan

[6] Research Guide, Ideal College of Pharmacy and Research, Kalyan

ABSTRACT: Acne is a skin condition that occurs when the hair follicles underneath the skin become blocked. Chamomile oil is a better treatment option for acne. Microspheres are made of synthetic and biodegradable polymers is a key to delivering the drug to the site of treatment in a controlled manner. The purpose of this is to formulate and evaluate chamomile microsphere loaded cream for enhanced topical delivery. The ionotropic gelation technique used to prepare the microsphere of Chamomile in which sodium alginate is used as polymer and calcium chloride as cross linker. The particle size and the entrapment efficiency of the microsphere formulation M1 and M2 was a consideration when evaluating it. The microsphere formulation that was optimized i.e M1 was put into cream that contained neem extract. It is found that, as polymer concentration increases particle size and entrapment efficiency also increases. Based on this study, it was concluded that the cream filled with Chamomile microspheres meets all the requirements of dosage forms that release the active ingredient in a controlled manner and studies encourage further clinical follow up and long term stability studies with this formulation.

***Keywords*:** Chamomile, Microsphere, Acne, Cream, Polymer.

INTRODUCTION :

Acne is so common that is considered as a normal part of puberty. But knowing that doesn't always make it easier if you've got a big pimple on your face. People with this acne prone skin claim more likely to experience low self-esteem, shame, and embarrassment. [1] Acne is a common skin condition that happens when hair follicles under the skin become clogged . People of all races and ages get acne, but it is most common in teens and young adults. When acne appears during the teenage years, it is more common in males . Acne can continue in adulthood and when it does it is more common in women. [2]

Reasons for acne development: The following factors may contribute to the appearance of acne.

- An overabundance of oil produced in the pores.
- The dead skin cells' accumulation inside the pore.
- Bacteria growing inside the pore.

Hormones : Acne may result from an increase in androgen, the hormones associated with male sex. In both boys and girls, these increases are typical of puberty lead to the enlargement and increased production of sebum by the sebaceous glands. Acne can sometimes be brought on by pregnancy related hormonal changes.

Family Background : It has been shown by researchers that having acne-prone parents may increase your risk of developing acne.

Prescription drugs : A number of drugs, including those containing lithium, corticosteroids, and hormones can bring on acne.

Age : Acne can affect people of any age, but it is most common in teenagers. A few more things that can exacerbate acne are:

Diet : Research indicates that consuming some meals may exacerbate acne. Environmental irritants such high humidity and pollution rubbing or squeezing imperfections.[3]

Types of acne :

There are various kinds of lesions or pimples that are caused by acne. There are various types of acne.

Whiteheads : A white lump caused by clogged hair follicles that remain under the skin's surface.

Blackheads : Obscured follicles that break open when they approach the skin's surface. Not because they are dirty, but rather because the sebum is discolored by the air, which is why they appear black.

Papules : Inflamed lesions that typically resemble little, pink pimples on the skin and may feel sensitive to the touch.

Pustules or pimples : Papules topped with pus-filled lesions that may be red at the base and white or yellow in colour.

Nodules : Massive, excruciating solid lesions buried deep in the skin.

Severe nodular acne : deep, painful, pus-filled lesions that are frequently referred to as cystic acne.[4]

Microspheres is a type of Novel drug delivery system for the skin formulation. The solid phase porous microsphere referred to as microsphere is a vehicle technology comprising inert , porous, polymer, spherical microparticles designed to entrap active ingredient , allowing for a slower rate of drug delivery into skin.[5]

Microsphere particles are also referred to as Microsphere beads or Microsponges. The process of its chemical manufacture involves the polymerization using specific inert monomers , which maybe selected on the basis of compatibility of the active ingredients. The active ingredients is the actual therapeutic agent which act therapeutically to treat the disease. [6]

The main advantages of using this microsphere drug delivery system is that it provides constant and prolonged therapeutic effect and reduces the dosing frequency and thereby improve the patient compliance. Also size of the microsphere is very important for the skin penetration ,therefore for effective absorption the size of the microsphere should be 5-50 micron . However < 100micron is also acceptable but not more than that. [7]

Here in this formulation we have used chamomile essential oil as our API. Chamomile oil is derived from the chamomile plant. Infact, chamomile is actually related to daisies. It is made from the flowers of the plant. There are two different varieties of chamomile such as Roman Chamomile (Chamaemelum nobile or Anthemis nobilis) and German Chamomile (Matricaria recutita or Chamomilia recutita) The active components of the chamomile contains terpenoids (bisoprolol , matricin, and chamazulene), Flavonoids (luteolin, rutin, and apigenin), hydroxycoumarins and mucilages.[8]

According to reports, essential oils derived from chamomile include antibacterial qualities that offer defense against specific kinds of bacteria ,fungi and viruses. Chamomile includes an antioxidant called apigenin which works to reduce inflammation by preventing the release of molecules that cause inflammation. Crushed chamomile was also said to be a great remedy for red inflamed skin. Chamomile also has astringent and brightening properties which helps in clearing pores and providing soft skin, it also helps in declining acne scars and hyperpigmentation when used regularly. [9]

The microsphere here in this formulation are loaded in a cream base which consist of neem extract which also contains antibacterial, anti-inflammatory and healing properties that shows effective pharmacological action on the acne prone skin. The cream base provide smooth application of microsphere on the skin also increasing its bioavailability and promote slow release of the drug from the formulation.

MATERIALS AND METHODS :

Materials :

Chamomile oil was used as the drug and neem powder , was purchased from nearby Ayurvedic Medical Store. Sodium alginate used as polymer, whereas Calcium chloride used as crosslinking agent for preparation of microspheres. All the other chemicals and reagents used in this project for preparation of microspheres and cream were of analytical grade and provided by college.

Methodology :

Preparation of extract : The neem powder was mixed with required quantity of ethanol and boiled until it get dissolved. Then the solution was cooled and filtered to get the neem extract.

Table 1 : Phytochemical screening of chamomile oil.

Test	Observation	Inference
Colour	Deep blue – green Colour	Chamomile present
Odour	Sweet, herbaceous, apple – like	Chamomile present
Solubility	Soluble in organic solvents	Chamomile present

Table 2 : Preliminary tests for neem powder .

Test	Observation	Inference
Colour	Yellowish green	Neem present
Odour	Characteristic odour	Neem present
Solubility	Soluble in organic solvents	Neem present

Table 3 : Phytochemical screening of neem.

Test	Observation	Inference
Test for terpenoids: 0.2g Drug extract is mixed with 2ml CHCL3 and 3ml Conc. H2SO4 was slowly added to form a layer	Reddish brown colour interface	Terpenoids are present
Test for flavonoids: Drug extract was mixed with 5ml ammonia and 1ml conc. H2SO4	Yellow colour which disappears on standing	Flavonoids are present

Preparation of microspheres :

Microspheres were prepared by using the method of ionotropic gelation, where sodium alginate is used as polymer and calcium chloride as cross-linking agent. Aqueous solution of Sodium alginate (2% w/v) was prepared. Then the required quantity of chamomile oil was added to the prepared 100ml solution of sodium alginate and mixed by magnetic stirrer. The obtained solution was extruded drop wise into 100 ml of aqueous calcium chloride solution (10% w/v) with the help of syringe and needle of small size while stirring using a magnetic stirrer. After stirring for 20 minutes, the obtained microspheres were filtered, washed with water and air dried.

Table 4 : Various formulations of microspheres

Ingredients	M1	M2
Chamomile oil	2ml	2ml
Sodium alginate	1g	2g
Calcium chloride	10g	10g

Figure 1 : Chamomile loaded microspheres

Preparation of microspheres loaded cream :

Materials :

Preparation of Chamomile microspheres loaded cream :

Materials – Neem Extract,

Chamomile oil,

Stearic acid,

Potassium hydroxide,

Methyl paraben,

Propyl paraben,

Glycerin,

Water

Procedure :

Stearic acid is weighed, mixed with Propyl paraben and heated in water bath and dissolved to prepare oil phase. Water phase is prepared by mixing water, potassium hydroxide, neem extract and methyl paraben and heated to 65°C. Both phases are heated to 65°C and then oil phase is added to the water phase and mixed till temperature lowers. The mixture was cooled at room temperature to get smooth cream. Formulated microspheres were uniformly dispersed into it.

Table 5 : Various formulations of microspheres loaded cream.

Ingredients	F1	F2
Chamomile oil loaded microspheres	5g	5g
Neem extract	2ml	2.5ml
Stearic acid	3.4g	3.8g
Potassium hydroxide	0.14g	0.14g
Methyl paraben	0.02g	0.02g
Propyl paraben	0.02g	0.02g
Glycerin	1ml	1ml
Water	Qs.	Qs.

Figure 2 : Microspheres loaded Cream

EVALUATION :

Evaluation of Chamomile microspheres :

Particle size analysis :

Optical microscopy method was used for the determination of average particle size of microspheres. Small quantity of microspheres were spread on a clean glass slide and average size of 20 microspheres was determined in each batch.[10]

Entrapment efficiency :

50 mg of microspheres were accurately weighed and crushed using glass mortar and pestle and then transferred to 100 ml of phosphate buffer pH 6.8 taken in a beaker. It was mixed by magnetic stirrer for few minutes. 1 ml of sample was withdrawn and make up to 10 ml using phosphate buffer pH 6.8. Absorbance was taken at 210 nm. and the concentration was calculated. [11]

Drug entrapment efficiency of the prepared microspheres was calculated in terms of percentage drug entrapment by using the formula,

% entrapment efficiency = (Practical drug content / Theoretical drug content) × 100

Evaluation of microsphere loaded cream :

Organoleptic evaluation : The formulated cream was evaluated for its organoleptic properties like odour, colour and state.

PH determination : PH meter was calibrated first. Then the pH of formulated creams was measured by using pH meter. [12]

Spreadability test : Required quantity of cream sample was placed on glass slides and spread the cream uniformly on the slide. The length and time which is required was taken and the spreadability was calculated by the formula,

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

Drug content : 1 g of formulated cream was dissolved in 100 mL phosphate buffer of 6.8pH by constant stirring. Then it was filtered and suitable dilutions were made using same buffer solution. Then absorbance was measured by UV spectrophotometer at 210 nm. [13]

RESULT AND DISCUSSION :

Particle size analysis : The results shows that the size of microspheres were found between the range from 173.8 to 347.6 µm. as shown in the table 3. From this, as the polymer concentration increases particle size also increases.

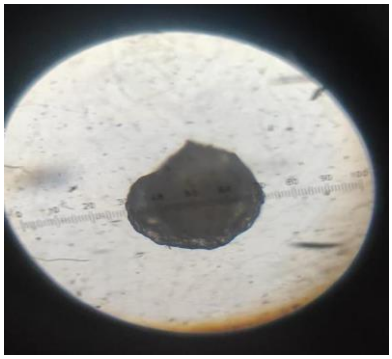
UV Spectroscopy : The absorbance value of the microsphere was found to be 0.138 at 210nm

Entrapment efficiency : The percentage entrapment efficiency of the microsphere formulations is shown in table 3 and was found to be in the range of 38-72.4%. From the result, maximum entrapment efficiency was found for M2. As the amount of polymer increases entrapment of drug within the microsphere also increases.

Table 6 : Particle size and Entrapment efficiency of microspheres.

Formulation	Particle size (µm)	Entrapment efficiency %
M1	173.8	38%
M2	347.6	72.4%

M1



M2

Figure 3 : Particle size of microspheres

Evaluation of microsphere loaded cream :

Physical properties : The cream has cream in colour, smooth texture , pleasant odour and homogeneous in nature.

PH determination : The PH of the cream was found to be 6.42 and 5.85 by using PH meter apparatus. The formulations shows pH which is suitable for skin as shown in the table 4.

Spreadability test : $S = (M \times L) / T$

The spreadability of different formulation of cream was found to be within the range of 4.53 to 5.89 g cm/s. Among this the best spreadable was found to be for F1.

UV Spectroscopy : The absorbance value of the microsphere loaded cream was found to be 0.332 at 210nm.

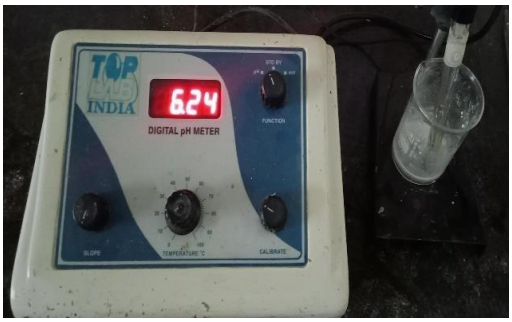
Drug content : The percentage drug content of the formulation was found to be in the range of 46.6% to 53.% By comparing F1 has good drug content.

Stability test : The microsphere loaded cream was kept for 90 days at room temperature. It was found to be stable at room temperature.

Table 7 : Spreadability and Drug content of microsphere loaded cream.

Formulation	pH	Spreadability (g cm/s)	Drug content %
F1	6.42	5.89	53.9%
F2	5.85	4.53	46.6%

F1



F2

Figure 4 : pH of microspheres loaded cream

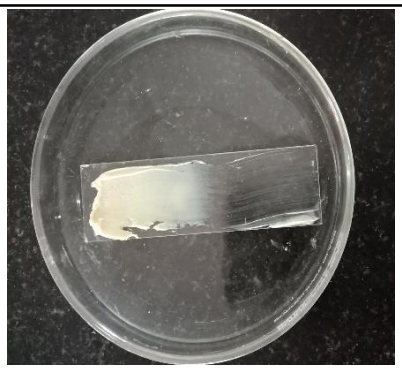


Figure 5 : Spreadability of microspheres loaded cream (F1)

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