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To Formulation and Evaluation of Minoxidil Microencapsulation

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ABSTRACT:

Minoxidil, a potent Blood pressure, stroke, and hair growth stimulant, presents challenges in stability and controlled release when formulated for topical application. Microencapsulation offers a promising strategy to overcome these hurdles. This study aimed to formulate minoxidil-loaded microcapsules using the coacervation method and evaluate their physicochemical properties and release characteristics. The microcapsules were prepared by phase separation induced by the interaction of sodium alginate and calcium chloride as the wall materials. Various formulations were investigated to optimize encapsulation efficiency, particle size, and drug release profile. The microcapsules were characterized for morphology, encapsulation efficiency, drug loading, particle size distribution, and stability. The analyse drug with thin layer chromatography and UV-spectrometry confirmed the compatibility of minoxidil with the wall materials and its stable encapsulation within the microcapsules. The developed microencapsulation technique offers a promising approach for enhancing the stability and efficacy of minoxidil in topical formulations for blood pressure, stroke, and hair growth promotion.

Keywords: Minoxidil, Sodium alginate, TLC (Thin layer chromatography), UV-spectrometry, Coacervation phase separation method.

Introduction:

Blood pressure is the lateral pressure exerted by the column of blood against the arterial walls. Types of blood pressure systolic blood pressure- the pressure of the blood as result of contraction of the ventricles and its cause the stroke. Diastolic blood pressure when the ventricles are at rest. Healthy blood pressure for men of age 18-39 is 119/70 mm Hg and that of women is 110/68 mm Hg. Healthy blood pressure for men of age 40-56 is 124/77 mm Hg and that of women is 122/74 mm Hg. Healthy blood pressure for men of age 60+ is 133/69 mm Hg and that of women is 139/68 mm Hg [1,2].

The process of packaging solid, liquid, or gaseous active substances inside another material in order to protect them from the environment is known as microencapsulation. As a result, active component is referred to as the core material, and the surrounding material as the shell. This method has been used in many different industries, including printing, chemicals, and pharmaceuticals [3]. The physical and chemical characteristics of the material to be enclosed determine the microencapsulation process. These micro-encapsule offer several advantages, including better material handling capabilities, environmental protection, the ability to separate reactive substances, and the ability to transform liquids into solids [4]. Minoxidil: - Active Pharmaceutical Ingredient. Sodium Alginate: - Thickening agent, gelling agent, emulsifier, stabilizer, texture improver. Calcium Chloride: - Crosslinking agent.

Aim:

The aim of the research is to formulation and evaluation the minoxidil microencapsulated by using coacervation phase separation method for the purpose of prevent blood pressure, stroke and hair losing.

Objective:

1. To developed new dosage form.
2. To evaluate the stability of the release rates of drug.
3. Identify which one of these mixtures is better to preserve its AOA (Antioxidant Activity) as an alternative for a natural additive.
4. To protect reactive substances from the environment.

Materials and Methods:

Materials:

Minoxidil-Purchased by **Swapnroop drugs and Pharmaceuticals** Address-Plot No:D-187/16, Five Star Shendra MIDC, Shendra, Aurangabad-431154, Maharashtra, India.

Sodium alginate- Purchased by **Shri Dayo Scientific Sales** 108, Anand Plaza, 1st Floor, Nashik-Poona Road, Near Vidyut Bhavan, Nashik Road-422101.

Calcium chloride- Purchased by **Shri Dayo Scientific Sales** 108, Anand Plaza, 1st Floor, Nashik-Poona Road, Near Vidyut Bhavan, Nashik Road-422101.

Methanol- Purchased by **Shri Dayo Scientific Sales 108**, Anand Plaza, 1st Floor, Nashik-Poona Road, Near Vidyut Bhavan, Nashik Road-422101.

Ammonia Solution- Purchased by **Shri Dayo Scientific Sales 108**, Anand Plaza, 1st Floor, Nashik-Poona Road, Near Vidyut Bhavan, Nashik Road-422101.

Methods

Analytical Methods

A. Thin Layer Chromatography:

Selection of Solvent:

The selection of the proper methods depends on the nature of the sample and its solubility [20,21]. To developed the chromatography method for the analysis minoxidil were performed by using methanol, ammonia solution to dissolved the minoxidil drug [5,6].

Preparation of solution:

To prepare 0.1% w/v solution of minoxidil in methanol.

Preparation of mobile phase solution:

The take 20 ml methanol and 0.3 ml of strong ammonia solution.

Procedure for estimation by TLC method:

The apply to the plate silica gel G solution. After development, dry the plate in air and examine under ultraviolet light. The principal spot in the chromatogram obtained with the solution corresponds to that in the chromatogram obtained with the reference solution [5,6].

Chromatographic condition:

Chromatographic parameter	Condition
Mobile phase	Methanol: Strong ammonia (20:0.3) %w/v
Stationary phase	Silica gel G
solution	0.1 percent w/v
visualization	Ultra violet fluorescence analysis cabinet
Visualization wavelength	254nm

Table no.1 Chromatographic condition

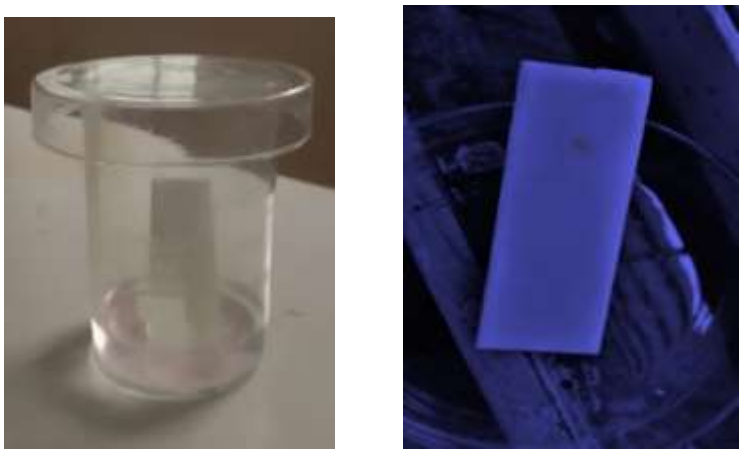


Fig no.1: Thin layer chromatography

B. UV Spectrophotometry Method:

Single pan electronic balance, UV visible spectrophotometer, UV visible double beam spectrophotometer, matched quartz cells corresponding to 1 cm path length. Pure sample of minoxidil were obtained from Swapnroop drugs and Pharmaceuticals Address-Plot No:D-187/16, Five Star Shendra MIDC, Shendra, Aurangabad-431154, Maharashtra, India.

Fig no.2: UV Spectrophotometry

Reagents: Methanol, water and minoxidil.

Preparation of standard stock solution:

The standard stock solution of drug was prepared by dissolving 10 mg of the drug in 10 ml standard flask using methanol as a solvent to give a concentration of 1000µg/ml. this stock solution on further dilutions were made to get 2µg/ml by using water as solvent [7,8].

Fig no.3: Standard solution

Preparation of sample:

The take 1 ml standard solution. Transferred in to a 100ml volumetric flask, and then make up with methanol. From that 1 ml of solution was transferred by 100ml volumetric flask the make volume with water yields a sample solution having a concentration assumed to be 1,2,3,4 and 5µg/ml of minoxidil [5,6].

Fig no.4: Test Solution

Method:

A. Coacervation phase separation method: Coacervation phase separation refers to partial homogeneous polymer solution into polymer-rich phase (coacervate) and the poor polymer phase (coacervation medium). Coacervation involves the separation of a liquid phase of coating material from a polymeric solution and wrapping of that phase as a uniform layer around suspended core particles [9,10].

Steps of coacervation:

1.Formation of three immiscible chemical phases.

2.Deposition of the coating

3.Rigidization of the coating

- **Step:1**

The formation of three immiscible chemical phases:

- A liquid manufacturing vehicle phase
- A core material phase
- Coating material phase
- To form the three phases, the core material is dispersed in a solution of the coating polymer, the solvent of the polymer being the liquid manufacturing vehicle phase. The coating material phase (an immiscible polymer in a liquid state) is formed by utilizing one of the methods of phase separation-coacervation,
- That is, by changing
- The temperature of the polymer solution
- Adding a salt
- Nonsolvent
- Incompatible polymer to the polymer solution
- Including a polymer-polymer interaction[17,18,19]

- **Step:2**

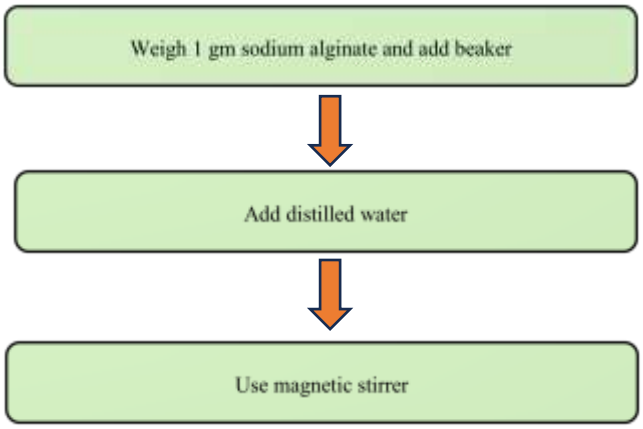
- Consists of depositing the liquid polymer coatings upon the core material. this is accomplished by controlled, physical mixing of the coating material (while liquid) and the core material in the manufacturing vehicle.
- Deposition of the liquid polymer coating around the core material occurs if the polymer is adsorbed at the interface formed between the core material and the liquid vehicle phase, and adsorption phenomenon is a prerequisite to effective coating.
- The continued deposition of the coating material is promoted by a reduction in the total free interfacial energy of the system, brought about by the decrease of the coating material surface area during coalescence of the liquid polymer droplets[17,18,19].

➢ **Step:3**

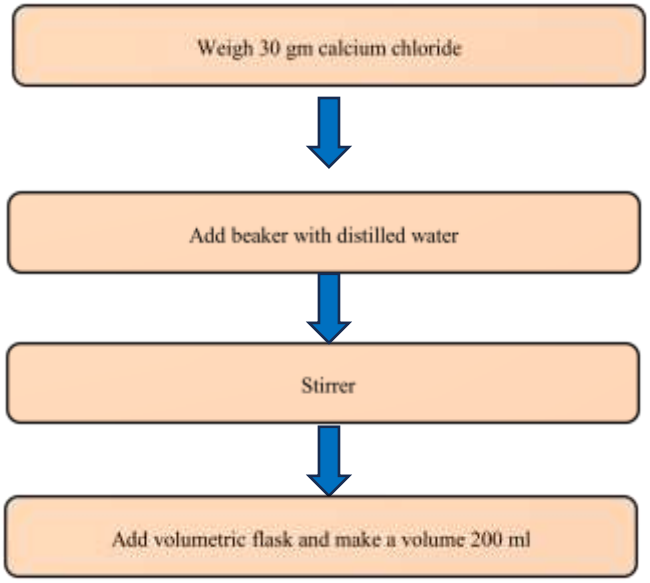
- Involves rigidizing the coating, usually by thermal, cross-linking, or desolations techniques, to form a self-sustaining microcapsule[17,18,19].

B. Preparation of microencapsulation:

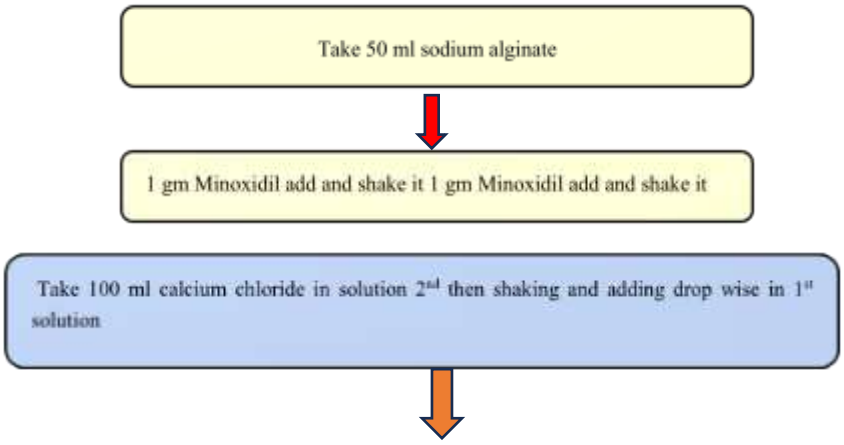
Solution 1:

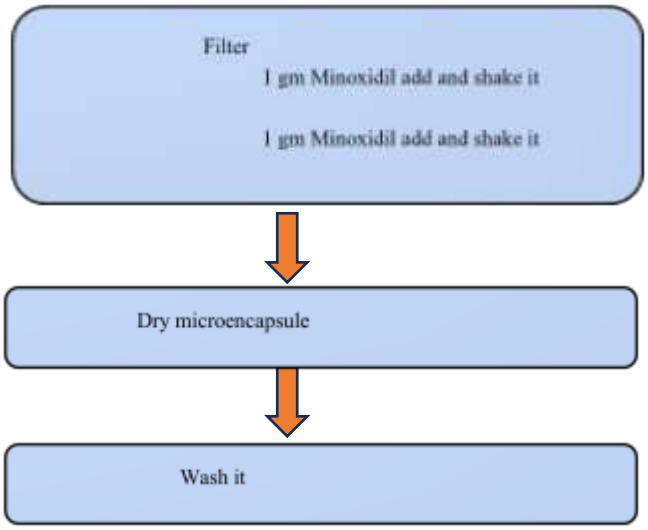


Solution 2:



Solution 3:





Formulation Table:

Sr.no.	Chemicals	Quantity	Uses
1.	Minoxidil	1gm	Active Pharmaceutical Ingredient
2.	Sodium alginate	1gm	gelling agent, texture improver
3.	Calcium Chloride	30gm	Crosslinking agent

Table no.2: Formulation table

Fig no.5: Micro-encapsules

Evaluation parameters:

Angle of repose:

1. Clean the all glassware's.
2. Weigh the 5 gm of Minoxidil powder
3. Powder pass from 10 mess sieve
4. Powder pass from set assembly of funnel with clamp or on ring support over a glass plate
5. Adjust the height of funnel at 5 cm

6. Place Minoxidil powder in funnel and block the tip of funnel in a figure
7. Remove your figure and flow powder in graph paper then using pencil in draw circle around loop
8. Repeat the procedure 1 to 4 times
9. Calculated angle of repose from radius and height [14,15,16].

tanǿ=h/r

Fig no.6: Angle of repose

Bulk density:

1. Clean all glassware's
2. Take 5 gm of Minoxidil powder
3. Add powder in measuring cylinder
4. Set up the density check the bulk volume
5. Calculate the bulk density [14,15,16].

$$bulk\ density = \frac{\text{mass}}{\text{bulk volume}}$$

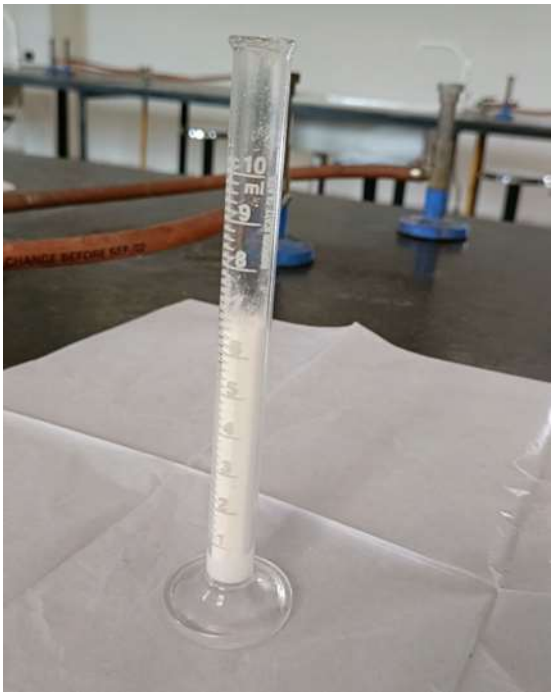


Fig no.7: Bulk Density

Tapped density:

1. Clean the glassware's
2. Take 5 gm of Minoxidil powder
3. Add powder in measuring cylinder
4. Set up the density apparatus
5. Tapped to 50 to 100 times
6. Make on tapped volume
7. Calculated the tapped density [14,15,16].

$$tapped\ density = \frac{\text{mass}}{\text{tapped volume}}$$

Fig no.8: Tapped Density

Carr`s index:

$$carr`s = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times$$

Hausner`s ratio:

$$Hausner`s\ ratio = \frac{\text{tapped density}}{\text{bulk density}}$$

Sieve Analysis:

- Separation of the microsphere into various size fractions can be determined by using a mechanical sieve shaker.
- A series of five standard stainless-steel sieve (20,30,45,60 and 80 mesh) are arranged in the order of decreasing aperture size.
- Five grams of drug loaded microspheres are placed on the upper-most sieve.
- The sieves are shaken for a period of about 10 min, and then the particle on the screen is weighed [13].

Fig no.9: Sieve Shaker

Morphology:

- The surface morphologies of microspheres are examined by a scanning electron microscope [11,12].

Fig no.10: Morphology study

Capture efficiency:

- The capture efficiency of the microspheres or the percent entrapment can be determined.

- The sample is then subjected to the determination of active constituents as per monograph requirement [12].
- The percent encapsulation efficiency is calculated using equation:

$$\%Entrapment = \frac{actual\ content}{\text{theoretical content}} \times 100$$

Beaker Method:

- The dosage form in these methods is made to adhere at the bottom of the beaker containing the medium and stirred uniformly using overhead stirrer.
- Volume of the medium used in the literature for the

-studies varies from 50-500ml

-stirrer speed form 60-300rpm.

Fig no.11: Beaker Method

Determination of Coating Polymer on Microcapsules

About 1 g of the microcapsules was accurately weighed and washed 3 times with 10 mL of acetone in order to remove polymer coating. The remaining drug-resinate core was dried at 50°C for 12 h and weighed. The percentage of coating polymer was calculated by the following equation [12]:

Percentage coating polymer = (Microcapsules weight − Dried complex weight/Microcapsules weight) × 100.

Stability Studies

The intermediate stability studies were carried out on the most satisfactory formulations according to ICH guidelines. The formulations were sealed in aluminium packaging and kept in stability chamber maintained at 30 ± 2°C/65% RH for one months.

Fig no.12: Stability study

Result:

- **Thin Layer Chromatography**
  - RF Value= o.87
- **UV Spectrometry**
  - ƛmax= 280nm.

Table no.3: Preformulation study result

Sr.no.	Parameters	Ranges	Properties
1	Angle of repose	35	Good
2	Bulk density	o.71	Excellence
3	Tapped density	0.83	Excellence
4	Carr`s Index	14	Excellence
5	Hausner ratio	0.85	Excellence

- **Sieve Analysis:**

Sieve no.	Weight
20	30mg
30	40 mg
45	60mg
60	100mg
80	20mg

Table no.4: Sieve Analysis

- **Morphology Study:**

The microencapsules are obtained various shapes such as spherical, cylindrical, or irregular, and their surface is smooth or rough. Analyzing their morphology with their structure.

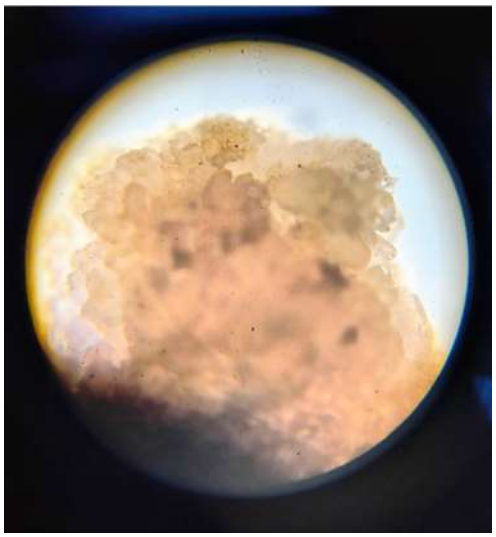


Fig no.13: Morphology study Result

- **Capture efficiency:**

$\%Entrapment = 90\%$

- **Beaker Method:**

The result of the beaker method in microencapsulation typically in the formation of microencapsules and the core material is encapsulated within a protective coating.

- **Determination of Coating Polymer on Microcapsules:**

Percentage coating polymer= 80%

- **Stability Studies:**

The micro-encapsule is stable with 60◦C temperature.

Conclusion:

The present study is repeated that it is an appropriate method to encapsulate drug in to sodium alginate shells because of good entrapment efficiency and sustained release behaviour among the formulations are the result of the drug to polymer ratio employed. This result may suggest that potential application of sodium alginate microencapsules as a suitable sustained release drug delivery system and it decrease the frequency of dosing and improve the patient compliance in the treatment of blood pressure, stroke and hair loss.

Discussion:

Controlled release drug delivery systems are aimed at controlling the rate of drug delivery, sustaining the duration of the activity and targeting the delivery of the to a tissue. Among the various approaches, microencapsules are widely accepted for controlled release. Polymers and release retarding materials used as a coat play a vital role in controlling the drug release from the microencapsulation. The overall objective of the to developed new dosage form. To evaluate the stability of the release rates of drug. Identify which one of these mixtures is better to preserve its AOA as an alternative for a natural additive. To protect reactive substances from the environment. The analysis the method thin layer chromatography and UV spectrometry. The before formulation microencapsulation pre-formulation studies angle of repose, bulk density, tapped density, cars index, hausner ratio was performed. All the microencapsules were evaluated for sieve analysis, capture efficacy, dissolution, stability studies, morphology, beaker method, particle size determination. The well result was showing the microencapsules.

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