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Research Article

Formulation and Evaluation of Hydrogel for the Treatment of Acne

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A B S T R A C T

The aim of this work was to prepare and evaluate the topical hydrogel for the treatment of acne. Minocycline hydrochloride based hydrogel was prepared using the methyl cellulose gelling agent, the drug concentration was kept constant at 0.25%. The concentration of propylene glycol and methyl paraben was kept constant at 15% and 0.3%. The hydrogel formulation was evaluated for various physicochemical parameters like percentage drug content, spreadability and drug release. Formulation H9 was highest drug content 98.23±0.031% and drug released 90.96 ± 2.6% of the drug in 6hr. Out of these formulations H9 for hydrogel was selected to prepare final hydrogel formulation. Developed hydrogel (H9) were evaluated like drug content spredability, homogeneity, washability, pH etc. Developed hydrogel formulation can be better effect to treat acne due to high drug retention and permeation in skin layers.

Keywords: Acne, Hydrogel, Minocycline Hydrochloride, In-Vitro Drug Releasew

Introduction

Acne is the inflammatory follicular disorder, approximately 85% affecting to the teenagers and 95% of the population suffers from acne. Endogenous and exogenous hormones respond to acne. It is pilosebaceous units, on the skin consisting of the open follicle, the group of sebaceous gland surround on that.

Acne is the common skin disease.[1] Acne is a cutaneous pleomorphic situation of the pilosebaceous component involving the unbalance in sebum production.

Acne is categorised by the inflammatory and non-inflammatory lesions. Acne is mainly cause by the propionibacterium and staphylococcus bacteria, present in the epidermis and pus form on the skin. Propionibacterium and staphylococcus bacteria are responsible for the several lesions of the acne.[2]

It is also called pimples, zits or blemishes. Several clinical management included seborrhoea, comedones, erythematous papules and pustules, less frequently nodules, deep pustules or pseudocysts, final scarring in few of them. Acne has four main pathogenic mechanism- abnormalities in sebum production, follicular hyperkeratinisation, Propionibacterium acne (P. acne) colonization, the products of inflammation.[3]

Minocycline is a broad-spectrum tetracycline. Tetracycline antibiotic that is fight bacteria in to body. Minocycline hydrochloride helpful in the bacterial infections, such as urinary tract infections, respiratory infections, skin infections, severe acne, gonorrhea, tick fever, chlamydia.[9] It is a bacteriostatic antibiotic, categorized as a long-acting type, results of its long half-life it normally has serum levels 2-4 times that of the simple water-soluble tetracyclines.[7,8]

Material and Method

Minocycline-hydrochloride was gift sample from Sun Pharma Ltd Dewas, agar, methylcellulose, methyl paraben, triethnolamine, propylene glycol, distilled water.

Preformulation Study

Preformulation study can be defined as analysis of physicochemical properties of drug substance alone and when combined with excipients. Investigation of Preformulation parameters is intended to find those physicochemical properties that may influence the formulation design, method of preparation and pharmacokinetic profile of resulting product.

The Preformulation studies performed for identification (Organoleptic properties, melting point, IR spectra, UV spectrum), solubility profile, partition coefficient, drug excipient interaction, quantitative estimation of drug etc.

Test for Identification

Organoleptic properties of drug

A small quantity of drug powder was taken on butter paper and observed in well illuminated place.

Table 1.Organoleptic properties of drugs

S. No.	Drug	Observation		
		Color	Odor	Taste
1.	Minocycline hydrochloride	Yellow color	Odourless	Bitter

Melting Point

The melting point of drug was determined by using open capillary method. Drug was filled into capillary then close. That tube was placed in the melting point determining apparatus and temperature rage at which powder started to melt to complete melting was observed.

Table2.Melting point

S.No.	Drug	Observation
1.	Minocycline hydrochloride	205-209

Solubility

Aquantitative estimation of the solubility was made by adding solvent in small incremental amount to a test tube containing fixed quantity of solute. After each addition, the system was vigorously shaken and observed visually.

Table 3.Solubility Profile Minocycline Hydrochloride

S.No.	Solvents	Minocycline hydrochloride Solubility
1.	Distilled water	48mg/ml
2.	Dimethyl sulfoxide (DMSO)	5mg/ml
3.	Methanol	2mg/ml
4.	Ethanol	4mg/ml

Partition Coefficient

Partition coefficient of drug was determined in solvent system n-octanol/ distilled water. 50mg of drug was dissolved in 50ml of water which was taken in separating funnel and 50ml of n-octanol was added to it. Funnel was shaken for 30min then separating funnel final isolation of two phases were carried out by using the separating funnel were kept overnight for separation. The content of both phase were separated. After appropriate dissolution, the aqueous phase was analysed against reagent blank solution using Shimadzu 1800 UV spectrophotometer and absorbance was measured. The drug concentration in n-octanol phase is determined by subtracting the amount in aqueous phase from the total quantity of drug. The partition coefficient value P was calculated by following equation in below:

$P_{o/w} = C_{oil} / C_{water}$

Where, $P_{o/w}$ = Partition coefficient

C_{oil} = concentration of drug in octanol

C_{water} = concentration of drug in water

Table 4.Partition coefficient of drug Mean±S.D (n=3)

S. No.	Drug	Observation
1.	Minocycline hydrochloride	0.03 ± 0.011

Drug Excipient Interaction Studies

Drug powder was mixed with various excipients in the ration of 1:1 and the resulting physical mixture was kept in sealed glass vials. These vials were placed at different temperatures conditions for 2 weeks. There was no change in the physical appearance like color change, lump formation of the mixture of drug and excipients. This indicated that the drug was compatible with all the formulation ingredients. Therefore there was found no change in the content of each vial in their physical characteristics.

Preparation of Hydrogel

Distilled water in added methyl cellulose placed over a night then 0.25gm of minocycline hydrochloride and added propylene glycol, methyl paraben for the preservative, hydrogel neutriliazed with triethnolamine. All the trial batches of hydrogel were evaluated by various parameters like appearance, pH, washability, viscosity, spredability, homogeneity, drug content.

Evaluation of hydrogel

- **Drug content:** The hydrogel sample (1gm) was withdrawn and dissolved in 100ml of phosphate buffer (pH 7.4). The volumetric flask containing hydrogel solution shaken for 2hr. This solution was filtered and estimated using UV spectrophotometer at 294 and 384nm

Table 5.Formulation Batches for Hydrogel

Formulation batches	Minocycline hydrochloride(mg)	Methyl Cellulose (gm)	Propylene glycol (ml)	Methyl paraben (gm)	TEA (ml)	Distilled water
H1	0.25	1	5	0.3	Qs	100
H2	0.25	2	5	0.3	Qs	100
H3	0.25	3	5	0.3	Qs	100
H4	0.25	1	10	0.3	Qs	100
H5	0.25	2	10	0.3	Qs	100
H6	0.25	3	10	0.3	Qs	100
H7	0.25	1	15	0.3	Qs	100
H8	0.25	2	15	0.3	Qs	100
H9	0.25	3	15	0.3	Qs	100

- **Measurement of pH:** The pH of various gel formulations was determined by using digital pH meter. One gram of hydrogel was dissolved in 100 ml distilled water and stored for two hours. Themeasurement of pH of each formulation was done in triplicate and average values are calculated
- **Spreadability:** A sample of 0.5 g of each formula was pressed between two slides (divided into squares of 5 mm sides) and left for about 5 minutes where no more spreading was expected. Diameters of spreaded circles were measured in cm and were taken as comparative values for spreadability. The results obtained are average of three determinations
- **Viscosity Estimation:** The viscosity of gel was determined by using a Brookfield DV-E viscometer model with a T-Bar spindle in combination with a helipath stand
- **Selection of spindle:** It is based on torque value. The torque % observed in viscometer with formulation. More than 10 torque value at different-different RPM decide the which spindle is best suited for formulation
- **Procedure of Brookfield:** Spindle wash with distilled water then ethanol and then dry. Spindle attaches with viscometer and then the probe of spindle is kept in gel. Then set spindle number on visual display and set RPM and start motor. Probe is not touch to glassware surface which contain formulation
- Then observed torque value. At optimum torque % noted viscosity in cps unit. This operation done in three times and noted the mean viscosity
- **Measurement of viscosity:** The spindle (6) was used for determining the viscosity of the gels the factors like temperature, pressure and sample size etc. Which affect the viscosity was maintained during the process
- **Homogeneity:** After the hydrogel have been set in the container, all formulation of hydrogel were tested for homogeneity by visual inspection. They were tested for their appearance and presence of any aggregates
- **Visual inspection:** All formulated hydrogel formula were checked for their homogeneity, color and presence of lumps by visual inspection after the gels have been set in the container
- **Extrudability study:** The hydrogel were set in the container, the formulations were filled in the collapsible tubes. The extrudability of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm. ribbon of gel in 10 second
- **Drug release:** The hydrogel in release of drug was determined by using the dialyis membrane mounted on the one end of open tube, containing 1gm of hydrogel. The dialysis tube was suspended in 200ml beaker containing 100 ml of PBS (pH 7.4)
- **Washability:** Hydrogelformulation was applied on the skin and then ease and extent of washing with water were check manually[12]

Result and Discussion

Minocycline Hydrogel Evaluation

Drug content

Results of drug content are shown in graph. After various formulation of minocycline hydrogel the drug content of the formulated gel (H9) was estimated and the results were range of81.23 $\pm$ 0.132 to 98.23 $\pm$ 0.031 %.

The drug content determination also showed that the drug was uniformly distributed throughout the gel. The drug content of formulation H9 showed highest drug content percentage.

Measurement of pH

The pH of the minocycline hydrogel was found in between 6.7 to 6.9. This pH is found to be close with the pH of human skin and hence it can be assumed that no skin irritation will occur after application of gel.

Table 6.Drug content, pH, Spreadability, Viscosity, Extrudability, Washability Mean±S.D (n=3)

Formulation batch	Drug content	pH	Spredabiility(gm.cm/sec)	Viscosity(cps)	Extrudability	Washability
H1	81.23 ± 0.132	6.7	3.9 ± 0.22	20643 ± 0.012	+	+
H2	85.46 ± 0.033	6.8	3.8 ± 0.10	22001 ± 0.031	+	++
H3	83.54 ± 0.024	6.9	3.7 ± 0.21	23431 ± 0.023	++	++
H4	86.64 ± 0.031	6.7	3.9 ± 0.33	23314 ± 0.033	+	+
H5	87.16 ± 0.023	6.8	4.1 ± 0.32	23547 ± 0.021	+	+
H6	88.49 ± 0.014	6.7	3.8 ± 0.11	23900 ± 0.031	++	++
H7	90.56 ± 0.012	6.7	4.0 ± 0.23	23600 ± 0.024	+	+
H8	95.45 ± 0.014	6.9	4.1 ± 0.12	24000 ± 0.021	+	+
H9	98.23 ± 0.031	6.8	4.2 ± 0.32	24200 ± 0.121	++	++

Excellent: +++, Good: ++, Average: +

Spreadability

The spreadability is very much important as show the behavior of gel comes out from the tube. The values of spreadability shown in table indicate that polymer used gave gels spread by small amount of shear. The diameters of the spreaded circles ranged from 3.7 ± 0.21 to 4.20.32gm. cm/sec.

Spreadability acting a significant role in patient compliance and facilitate in regular application of gel to the skin. A good gel takes less time to spread and will have elevated Spreadability. The spreadabilty of formulated gel was decreased as the concentration of gelling agent increased.

Viscosity

Brookfield digital viscometer was used to measure the viscosity (in cps) of the prepared gel formulation. The spindle no. 6 was rotated at 10 rpm. The torque % of the formulation was near to 30%. Reading was detected 30 sec after measurement was made, when the level was stabilized.

Viscosity is an essential parameter for characterize the gels as it effect the spreadability, extrudability and release of the drug, all formulated gels showed in increased viscosity as the concentration of the gelling agent was increased.

Homogeneity

Visual Examination

The prepared gel of H1 to H9 formula was inspected visually for their color and syneresis. The developed preparation of H9 is much clear and transparent. The developed gel H9 showed good homogeneity with absence of lumps and syneresis.

Physical stability study of formulation

The prepared hydrogel formulation was stored at room temperature and refrigeration for a period of 30 days and then visually observed for clearance of every week.

Table 7.Minocycline Hydrochloride Release from hydrogel Mean±S.D (n=3)

Time [hr]	% Cumulative Drug Release
15min	15.352 ± 1.76
30min	20.8 ± 1.83
1hr	37.352 ± 0.68
2hr	54.46 ± 2.1
4hr	68.04 ± 1.32
6hr	90.96 ± 2.6

Table 8.Physical Stability of Liposomal Hydro gel mean±S.D (n=3)

Conditions	Appearance	pH
Refrigeration (2-8)	Yellowish color	6.8
Room temperature	Yellowish color	6.9
40/75% RH	Yellowish color	6.7

Conclusion

The prepared hydrogel was evaluated for in-vitro drug release. Minocycline hydrochloride based hydrogel was prepared using the methylcellulose gelling agent, the drug concentration was kept constant at 0.25%. The concentration of propylene glycol and methyl paraben was kept constant at 15% and 0.3%. The hydrogel formulation was evaluated for various physicochemical parameters like percentage drug content, spreadability and drug release. Formulation H9 was highest drug content 98.23 ± 0.031% and drug released 90.96 ± 2.6% of the drug in 6hr. Developed hydrogel (H9) was evaluated like drug content and spredability, homogeneity, washability, pH etc. Developed hydrogel formulation can be better effect to treat acne due to high drug retention and permeation in skin layers.

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