RESEARCH ARTICLE

Formulation and Characterization of Ozenoxacin 1% Cream for Treatment of Impetigo

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ABSTRACT

A new cream has been developed those features 1% active oxenoxacin, a topical antibacterial that effectively kills gram-positive bacteria. It's specifically designed to tackle impetigo, which is a bacterial skin ailment that spreads easily. A cream with 1% ozenoxacin is in the works to tackle bacterial skin infections, especially impetigo, which affects both adults and kids (from two months old). This product is specifically designed for treating impetigo. The cream's inactive components are well-known and frequently seen in topical medications, chosen based on a study that looked at how they interact with the drug. Ozenoxacin is a novel, fast-acting topical antibiotic, has a good microbiological profile, and is considered safe. However, it's really important to use it responsibly and follow antimicrobial stewardship practices to keep this innovative treatment effective.

KEYWORDS: Topical cream, Antibiotics, Ozenoxacin, Impetigo.

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INTRODUCTION

The United States has approved Ozenoxacin, a novel nonfluorinated quinolone antibiotic, for the topical treatment of impetigo in adults and infants two months of age and more that has been brought on by S. aureus or S. pyogenes[1]. Ozenoxacin had potent bactericidal efficacy against Gram-positive pathology-relevant organisms, particularly streptococci and staphylococci[2], in contrast to a range of other antimicrobial drugs. Because oxenoxacin's chemical structure does not contain a fluorine atom, Compared to fluorinated quinolones, its safety profile is superior. Among these include the absence of chondrotoxic potential and a broader spectrum of action against S. aureus strains that are resistant to methicillin, mupirocin, and ciprofloxacin[3-5]. Impetigo is treated with ozenoxacin, a special synthetic quinolone antibiotic. The approved 1% topical cream formulation is effective in addressing this condition. This antibiotic is particularly valuable against certain bacteria that have shown resistance to fluoroquinolones. Young children are the main victims of impetigo, a highly contagious bacterial skin infection [6-8]. The global median prevalence is expected to be 2.5 times greater for children than for adults. An estimated 3 million cases of impetigo are reported annually in the United States. Hot, muggy weather, socioeconomic hardship, crowded spaces, starvation, and specific lifestyle choices like playing close-contact sports are major risk factors for impetigo[9]. *Staphylococcus aureus* is the primary cause of impetigo, while *Streptococcus pyogenes*, either by itself or by conjunction with *Staphylococcus aureus*, is implicated as well. Erythematous pustules or vesicles, sometimes referred to as red sores, are the illness's hallmark. These swiftly develop into surface erosions with a distinctive honey-colored crust[10]. Although lesions usually only affect the hands, face, and neck, they can spread to other body areas by scratching or close contact. A special risk to educational institutions and childcare facilities is posed by Impetigo because of its high contagiousness. To stop the illness from spreading, Youngsters who have impetigo should stay at home for at least 24 hours following the proper antibiotic treatment, according to the American Academy of Paediatrics[11]. Clinical practice recommendations include treating localised impetigo patches with topical antibacterial drugs and treating systemic infections and many or extensive lesions that are not getting better when treated topically with oral medicines[12,13].

Topical ozenoxacin 1% cream was investigated for impetigo in adults and children in two phase-3 clinical trials with sufficient power and control13 and a phase-1 study[14]. The results demonstrated the medication's effectiveness and good tolerability. To further understand the clinical profile of ozenoxacin only in the pediatric population, data from participating children ages 2 months to under 18 years was gathered and examined. According to the European prescription for ozenoxacin, children and adolescents with nonbullous impetigo were included in a comparable study of paediatric patients in the same clinical trials[15, 16], which are aged from 6 months to less than 18 years, is complemented by this analysis.

MATERIALS AND METHODS

Active ingredient: Ozenoxacin (1% w/w)

Base: Hydrophilic cream base (e.g., carbomer, glycerin, and water)

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Table 1: Formulae for development of 1% Ozenoxacin creams

S.no	Ingredients	Trials (ingredients in grams)		
		C1	C2	C3
1	Methyl paraben	0.2	0.2	0.2
2	Glyceryl monostearate	5	2.5	5
3	Propyl paraben	0.1	0.1	0.1
4	propylene glycol	10	15	15
5	Emulsifying wax	5	2	4
6	Soft parafin	10	7	-
7	Ozenoxacin	1	1	1
8	Liquid parafin	-	3	10
9	Purified water	68.7	69.2	64.7

Table 2: Investigations into the physical properties of ozenoxacin

S. no.	Characteristic	Observation
1	Melting point	>255°C (dec.)
2	Boiling point	573.5±50.0 °C (Predicted)
3	Density	1.372±0.06 g/cm^3 (Predicted)
4	Partition coefficient of Ozenoxacin between octanol and water	2.2
5	Solubility	DMSO (Slightly)
6	Description	Off white colour powder

Excipients: Glyceryl monostearate (emulsifier and stabilizer), Liquid parafin (emollient), Emulsifying wax, Soft parafin, Purified water, etc.

Methods

Ozenoxacin is synthesized through a multi-step chemical process involving condensation, reduction, and purification.

Preparation of 1% Ozenoxacin creams

Three formulations of 1% ozenoxacin creams, designated C1, C2, and C3, were chosen from a series of formulation testing due to their appropriate consistency and spreadability. Their formulas are provided below table 1. Melting emulsifying wax, glyceryl monostearate, and soft paraffin in a china dish. The procedure was conducted over a water bath at 70°C. Propylene glycol had been used to dissolve ozenoxacin, which was then combined with liquid paraffin. After adding this combination to the melted mixture, the temperature was kept at 70°C. In a beaker filled with recently boiled and cooled water, methyl and propyl paraben were dissolved simultaneously while the temperature was kept at 70°C. Following a thorough swirl, the aqueous phase was introduced to the oily phase. In order to prevent aeration, the fluid combination was removed from the water bath and stirred until it cooled. Effective stirring was used to prevent any crystallisation of the substance [17,18].

Two types of analyses were performed on three batches of 1% Ozenoxacin creams: chemical and physical. There is marketed ozenoxacin cream available; it is designated as Marketed cream (MC). For their physical investigation, three batches of manufactured Ozenoxacin cream were compared to the cream that was marketed under that name. For additional research, the formulation that matched the marketed sample the best was selected.

Physical characteristics determination: The substance underwent the following physical characteristic investigations.

Description: The drug is observed visually for its color and nature.

Solubility

The temperature was adjusted to 20°C once the room temperature was noted. One hundred millilitres of solvent were put into a clean, dry beaker. This solvent was aggressively agitated when oxenoxacin was gradually introduced. One portion of oxenoxacin was added at a time until it was fully dissolved. This was a sign of saturation. After filtering this combination, the resultant material was collected. Ten millilitres of the filtrate were pipetted out, placed on a tar-covered porcelain dish, and weighed to find the weight of ten millilitres of the solution after the first twenty millilitres of the filtrate were rejected. The solution evaporated when heated to a regulated temperature that was just above or equal to the solvent's boiling point. The mixture was cooled to room temperature once controlled evaporation was completed in the last steps. The china dish is weighed once more to calculate the residual. They weighed the residue. To find the amount of solvent required to dissolve one gramme of solute at the given temperature, the following formula was adjusted by varying the weights.

Selection of cream base

The water in the oil emulsion is the result of the anhydrous bases, sometimes referred to as absorption type bases, having the capacity to absorb water. Examples of soap-type bases are triethanolamine and sodium bicarbonate. The type of surfactant cream that is used combines ionic and non-ionic surfactants. The method of emulsifying involves boiling water to 70°C and dissolving soluble components in it. The temperature is maintained at 70°C by melting bases all at once. The aqueous phase is then added to the oily phase and continually triturated until creams form.

In our study, an emulsifying wax base was used to create Ozenoxacin cream. The ratios of the cream base and other

Table 3: The physical characteristics of formulations containing 1% Ozenoxacin cream

S. No.	Properties	C1	C2	C3
1	Appearance (Scores)	4	6	8
2	Colour	White	White	White
3	pH	5.5	5.7	6.2
4	Viscocity	25500	25950	26200
5	Spreadability (g. cm/sec)	23	24	26
6	Extrudability (g)	520	530	545
7	Firmness (g)	680.45	692.8	703.5
8	Consistency (g)	2265.35	2354.6	2425.4
9	Cohesiveness (g)	-486.56	-506.56	-523.5
10	Hardness (g)	20.16	22.4	23.6
11	Stickiness (g)	-14.35	-15.36	-16.5

Table 4: *In-vitro* release studies of topical formulations of 1% Ozenoxacin

Formulation	Amount	% of Drug Release in Minutes						
		0	30	60	120	180	360	720
Cream (C3)	1g	0	28.3	37.3	59.7	73.5	82.1	89.8
Marketed Cream (MC)	1g	0	35.6	50.8	63.8	75.1	84.3	89.9

Table 5: Stability study of the formulations - 90 days

S. No.	Properties	C3	MC
1	Apperance	9	9
2	Colour	White	White
3	pH	6.3	6.4
4	Viscocity at 30°C	27341	26901
5	Spreadability (g.cm/s)	28	27
6	Extrudability (g)	537	546
7	Firmness (g)	780.2	790.17
8	Consistency (g)	2459.21	2582.54
9	Cohesiveness (g)	-513.54	-526.49
10	Hardness (g)	24.11	27.02
11	Stickiness (g)	-14.8	-14.22

excipients were permuted and combined to create several cream formulations. Based on physical inspection, three cream formulations were selected for further study because of their suitable consistency and spreadability.

Melting point determination

The melting point of a chemical is the physical property that is used to identify it or confirm its purity. The determination was made using the capillary method. The Ozenoxacin was applied to a clean surface. We used a capillary tube with one end open and the other closed. The open end of the capillary tube was inserted into the compound to fill it with medication. The capillary melting point tube was placed within the melting temperature apparatus. The temperature within the chamber was progressively raised. The sample was repeatedly observed. From the moment the sample started to melt until each sample turned liquid, the melting range of the sample was recorded.

Characterization of Ozenoxacin Cream

Organoleptic test

The samples' organoleptic properties were examined under the same temperature, lighting, and packaging conditions in order to assess differences in appearance, phase separation and colour.

pH measurements

Ten millilitres of distilled water were combined with one gramme of each mixture. After homogenisation, the sample's pH was measured using a pH meter.

Viscosity

To determine the viscosity, a Brookfield viscometer (Model LVDV III) was employed. The viscometer's "Standby Mode" is chosen. After giving the samples a good shake, they were let to reach room temperature. At 30°C, the viscosity of the sample is measured. We used centipoises to record the reading.

Spreadability

After being suitably modified in the laboratory, this made it possible to calculate the formulation's spreadability. We calculated the spreadability by-

$$S = \frac{M \times L}{T}$$

T = time taken in seconds
M = weight tied to the upper side
L = length of the glass slides
S = spreadability

The weight was progressively increased if, after 30 grammes, the slide did not move. We gradually reduced the weight if the slide was moving swiftly.

Evaluation of greasiness (Hardness and Stickiness)

With a trigger force of 5.0 gms and a fixed height of 10.0 mm, the samples were set up in an auto type trigger. Using a stainless steel probe with a diameter of 1 cm, two compression were made into the formulation at a speed previous from test is 2.0 mm/sec and the speed during test is 1.0 mm/sec at a distance of 20 mm. From 20 mm, the post-test velocity remained steady. The program used for both data collection and calculation was called XTRA Dimension.

Stability study of the formulations

The ideal combinations were stored at 25°C ± 2°C in a 10-gram collapsable tube. Samples from each formulation were taken out at predetermined intervals of 30, 90 days in accordance with ICH guidelines.

RESULTS AND DISCUSSION

Determination of Physical characteristics

The investigations into the physical characteristics of ozenoxacin were carried out following the outlined methodology and are presented in Table 2.

Physical examination of the trail formulations containing 1% Ozenoxacin.

Physical and mechanical properties, such as appearance, color, pH, viscosity, spreadability, extrudability, firmness, consistency, cohesiveness, hardness, and stickiness, were assessed for the experimental formulations of oxenoxacin C1, C2, C3, and MC. Commercially available product or its bases were compared to the formulations' physicochemical properties. The best formulation was determined to be the one that most closely resembled the advertised product or base. Formulation C3 (cream) was shown to be the most advantageous. Table 3 displays the following physical attributes of the 1% Ozenoxacin cream formulations

In-vitro release studies of Ozenoxacin

Following the described protocol, the in-vitro release experiments were conducted for both the commercially available Ozenoxacin formulation and the other formulations. The percentage of drug release is shown in Table 4. Using a UV spectrophotometer, topical formulations of 1% Ozenoxacin cream were subjected to in-vitro release experiments. The outcomes were compared. It was discovered that the release had first-order kinetics.

Dermal tolerability

Active ingredient and/or excipients most probably produce

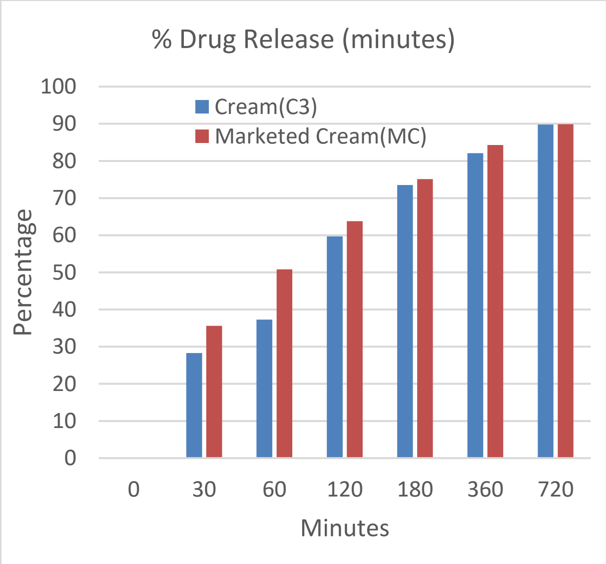

Figure 1: Percentage drug release in Minutes

skin irritation, also known as sensitization, is known as dermal tolerability. is a crucial consideration when developing topical formulations. The possibility of causing phototoxic or photosensitive reactions must also be assessed due to the possibility of applying topical treatments to skin regions that are vulnerable to exposure to sunlight.

Stability studies of the selected formulations as per ICH guidelines

Temperature-controlled collapsable tubes maintained at 25°C ± 2°C, were used to evaluate the stability of the best formulas and those that were on the market. In compliance with ICH norms, samples were taken at several intervals, particularly at 90 days, and underwent the specified physical and chemical examinations. Table 5 presents the results of the stability investigation, which was carried out in accordance with the established procedure.

CONCLUSION

A more recent topical antibiotic with a favourable microbiological profile, quicker clinical activity, and safety is oxenoxacin. However, antimicrobial stewardship and avoiding indiscriminate use are necessary to preserve the usefulness of this novel drug. Ozenoxacin cream appears to remain in the epidermis mainly on stratum corneum which are the top layers of skin, and does not readily permeate the dermis, the lowermost layer of skin. The formulations of oxenoxacin cream exhibit no signs of irritation, sensitisation, phototoxicity, or photoallergic reactions. When given to adults, ozenoxacin 1% cream has a favorable safety and tolerability profile, but children with impetigo, it does not absorb well.

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