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Review Article

A Review -Microsponges For The Treatment Of Acne Vulgaris

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ABSTRACT

Acne vulgaris is a common dermatological condition that affects a significant portion of the population, particularly adolescents and young adults. The need for effective topical treatments has led to the exploration of novel drug delivery systems. This study focuses on the formulation and characterization of nadifloxacin-loaded microsponge systems aimed at enhancing the therapeutic efficacy and skin penetration of the drug. Nadifloxacin, a potent topical antibiotic, is known for its effectiveness against acne-causing bacteria but is limited by its poor skin permeation and stability. Microsponge technology offers a promising approach to overcome these limitations by providing a controlled release mechanism and improving the bioavailability of the drug. In this research, nadifloxacin-loaded microsponges were prepared using a solvent evaporation technique, employing various polymers to optimize the formulation. The microsponges were characterized for their particle size, morphology, drug loading efficiency, and in vitro release profiles. The results demonstrated that the formulated microsponges exhibited a uniform size distribution and spherical morphology, with a high drug loading capacity. In vitro release studies indicated a sustained release of nadifloxacin over an extended period, suggesting the potential for prolonged therapeutic action. Furthermore, the stability of the microsponges was assessed under different storage conditions, confirming their viability for topical application.

INTRODUCTION

Acne Vulgaris –

Acne vulgaris is the formation of comedones, papules, pustules, nodules, and/or cysts as a result of obstruction and inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Acne develops on the face and upper trunk. It most often affects adolescents. Acne vulgaris is a skin condition that occurs when hair follicles are blocked with dead skin cells, bacteria, and oil (sebum). The blocked follicles cause blemishes on the skin, including pimples, blackheads, whiteheads, and cysts. Also known as common acne, one of its main causes is hormones, especially around puberty. (Williams HC et.

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al.2012) Acne is a multifactorial inflammatory disease affecting pilosebaceous follicles. The initial event in the development of an acne lesion is abnormal desquamation of the keratinocytes that line the sebaceous follicle, which creates a microplug or microcomedo. An increase in circulating androgens at the onset of puberty stimulates the production of sebum into the pilosebaceous unit. These events combine to create an environment within the pilosebaceous unit that is favorable for the colonization of the commensal bacteria, Propionibacterium acnes. With proliferation, P acnes secrete various inflammatory molecules and chemotactic factors that initiate and perpetuate the local inflammatory response and possibly induce keratinocyte hyperproliferation as well. (Williams HC et. al.2012) During puberty, under the influence of androgens, sebum secretion is increased as 5-alpha reductase converts testosterone to more potent DHT, which binds to specific receptors in the sebaceous glands increasing sebum production. This leads to an increased hyperproliferation of follicular epidermis, so there is retention of sebum. Distended follicles rupture and release pro-inflammatory chemicals into the dermis, stimulating inflammation. C.Acnes, Staphylococcus epidermis, and Malassezia furfur induce inflammation and induce follicular epidermal proliferation. (Harper JC et.al2019)Acne occurs through the interplay of 4 major factors:

- Excess sebum production
- Follicular plugging with sebum a keratinocytes.
- Colonization of follicles by Cutibacterium acnes (formerly Propionibacterium acnes), a normal human anaerob
- Release of multiple inflammatory mediators

Acne can be classified as

Noninflammatory:

Characterized by comedones.

Inflammatory: Characterized by papules,pustules, nodules, and cysts (Harper JC et.al2019) The most common places where you might have acne are on your:

- Face.
- Forehead.
- Chest.
- Shoulders.
- Upper back.

Oil glands exist all over your body. The common locations of acne are where oil glands exist the most.

Fig.1. Types of Acne

TYPE OF ACNE-

Acne is a word that actually refers to a variety of blemishes that can occur on the skin. Breakouts may include one or a combination of the different types of acne vulgaris.

Comedonal –

comedonalacneis distinct a type of mild to moderate vulgaris acne. The produced on the skin consist first and foremost of blackheads and whiteheads, although, pustule and papules can present themselves as well.

Whitehead:

This is one type of blemish known as a comedone. Whiteheads look like small raised white or skin-colored bumps. They occur when oil and dead skin cells clog the pore. This is also known as closed-pore acne.

Blackhead:

With this type of comedone, the build-up of oil and dead skin widens the pore so it looks open. The substance in the pore reacts with oxygen to form a black color. This is known as open-pore acne.

Pustule:

When bacteria get trapped in a pore along with dead skin cells and oil, it forms a pimple. These may swell and look inflamed. If the pimple has pus inside, it's a pustule.

Papule:

If the pimple does not have pus, it is called a papule.

Nodule:

Nodular acne is a severe type of acne. Nodules are bigger than typical pimples. They go deep into the skin and cause inflammation.

Breakouts:

can be widespread and painful. In addition, nodules are hard to the touch and do not contain pus.

Cyst:

Cystic acne is another severe form of acne vulgaris. Like nodules, the pimples are inflamed and go deep into the skin. They can be very large and are filled with pus. (Harper JC et.al2019)

A. Mild acne :-

this consist of condition where the lesion are chiefly non- inflammatory with very a small number of inflammation lesion .generally less than ten in number, mild acne can additional be classified into two type , the mild comedonal acne where comedones acne where papules or pustules may be there but are very little in number(fewer than ten).

B. Moderate acne:-

In moderate acne there are various come done few or many pustules, few nodules but no major scarring. There may be extreme pigmentation of the skin in some in some cases and these lesions are frequently found on the face, shoulder, back and chest. This is usually treated with oral antibiotics and retinoid as well as hormones treatment in women.

C. Sever acne:-

In these cases, various pain full and inflammatory nodules are present all over body. There may be the incidence of innumeeerable papopustules (i.e. Small collection or pocket of pus).This typically results in scaring. For these patients are utilize of a combination of topical oral antimicrobial in proper. (Kultu O el.al. 2023)

SIGN AND SYMPTOMS –

Symptoms of acne on your skin include:

Pimples (pustules):

Pus-filled bumps (papules).

Papules:

Small, discolored bumps, often red to purple or darker than your natural skin tone.

Blackheads:

Plugged pores with a black top.

Whiteheads:

Plugged pores with a white top.

Nodules:

Large lumps under your skin those are painful.

Cysts:

Painful fluid-filled (pus) lumps under your skin.

Acne can be mild and cause a few occasional pimples or it can be moderate and cause inflammatory papules. Severe acne causes nodules and cysts.

CAUSE OF ACNE

Clogged hair follicles or pores cause acne. Your hair follicles are small tubes that hold a strand of your hair. There are several glands that empty into your hair follicles. When too much material is inside your hair follicle, a clog occurs. Your pores can clog with:

Sebum:

An oily substance that provides a protective barrier for your skin.

Bacteria:

Small amounts of bacteria naturally live on your skin. If you have too much bacteria, it can clog your pores.

Dead skin cells:

Your skin cells shed often to make room for more cells to grow. When your skin releases dead skin cells, they can get stuck in your hair follicles.

When your pores clog, substances plug up your hair follicle, creating a pimple. This triggers inflammation, which you feel as pain and swelling. You can also see inflammation through skin discoloration like redness around a pimple. (Kultu O el.al. 2023)

Four main factors cause acne:

- Excess oil (sebum) production
- Hair follicles clogged by oil and dead skin cells
- Bacteria
- Inflammation

Acne typically appears on your face, forehead, chest, upper back and shoulders because these areas of skin have the most oil (sebaceous) glands. Hair follicles are connected to oil glands.

Certain things may trigger or worsen acne:

- Hormonal changes. Androgens are hormones that increase in boys and girls during puberty and cause the sebaceous glands to enlarge and make more sebum. Hormone changes during midlife, particularly in women, can lead to breakouts too.
- Certain medications. Examples include drugs containing corticosteroids, testosterone or lithium.
- Diet. Studies indicate that consuming certain foods — including carbohydrate-rich foods, such as bread, bagels and chips — may worsen acne. Further study is needed to examine whether people with acne would benefit from following specific dietary restrictions. (Williams HC et.al.2012)
- Stress. Stress doesn't cause acne, but if you have acne already, stress may make it worse.

Risk factors

Risk factors for acne include:

Hormones and acne-

Acne is largely a hormonal condition that's driven by androgen hormones (testosterone). This typically becomes active during teenage and young adult years. You might also notice acne forming around the time of your period as a result of hormone activity. Sensitivity to this hormone — combined with surface bacteria on your skin and substances released from your body's glands — can result in acne.

TREATMENT FOR ACNE-

Acne medications work by reducing oil production and swelling or by treating bacterial infection. With most prescription acne drugs, you may not see results for four to eight weeks. It can take many months or years for your acne to clear up completely.

Topical medications

Azelaic acid and salicylic acid. Azelaic acid is a naturally occurring acid produced by a yeast. It has antibacterial properties. A 20% azelaic acid cream or gel seems to be as effective as many conventional acne treatments when used twice a day. Prescription azelaic acid (Azelex, Finacea) is an option during pregnancy and while breast-feeding. It can The most common topical prescription medications for acne are:

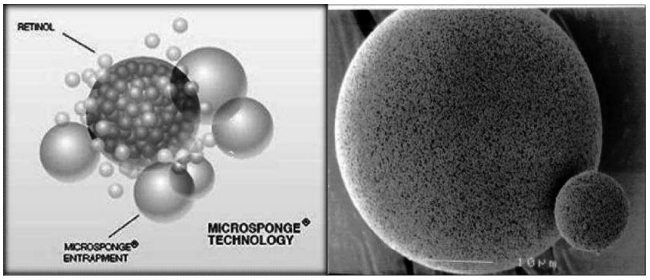
- Retinoids and retinoid-like drugs. Drugs that contain retinoic acids or tretinoin are often useful for moderate acne. These come as creams, gels and lotions. Examples include tretinoin (Avita, Retin-A, others), adapalene (Differin) and tazarotene (Tazorac, Avage, others). You apply this medication in the evening, beginning with three times a week and then daily as your skin becomes used to it. It prevents plugging of hair follicles. Do not apply tretinoin at the same time as benzoyl peroxide.
- Topical retinoids increase your skin's sun sensitivity. They can also cause dry skin and redness, especially in people with brown or Black skin. Adapalene may be tolerated best.
- Antibiotics. These work by killing excess skin bacteria and reducing redness and inflammation. For the first few months of treatment, you may use both a retinoid and an

antibiotic, with the antibiotic applied in the morning and the retinoid in the evening. The antibiotics are often combined with benzoyl peroxide to reduce the likelihood of developing antibiotic resistance. Examples include clindamycin with benzoyl peroxide (Benzaclin, Duac, others) and erythromycin with benzoyl peroxide (Benzamycin). Topical antibiotics alone aren't recommendedalso be used to manage discoloration that occurs with some types of acne. Side effects include skin redness and minor skin irritation. (Tropyet.al.,2004)

- Salicylic acid may help prevent plugged hair follicles and is available as both wash-off and leave-on products. Studies showing its effectiveness are limited. Side effects include skin discoloration and minor skin irritation.
- Dapsone. Dapsone (Aczone) 5% gel twice daily is recommended for inflammatory acne, especially in women with acne. Side effects include redness and dryness.
- Evidence is not strong in support of using zinc, sulfur, nicotinamide, resorcinol, sulfacetamide sodium or aluminum chloride in topical treatments for acne. (Tropyet.al.,2004)
- Oral medications-
- Antibiotics. For moderate to severe acne, you may need oral antibiotics to reduce bacteria. Usually the first choice for treating acne is a tetracycline (minocycline, doxycycline) or a macrolide (erythromycin, azithromycin). A macrolide might be an option for people who can't take tetracyclines, including pregnant women and children under 8 years old.
- Combined oral contraceptives. Four combined oral contraceptives are approved by the FDA for acne therapy in women who also wish to use them for contraception. They are products that combine progestin and estrogen (Ortho Tri-Cyclen 21, Yaz, others)
- Anti-androgen agents. The drug spironolactone (Aldactone) may be considered for women and adolescent girls if oral antibiotics aren't helping. It works by blocking the effect of androgen hormones on the oil-producing glands. Possible side effects include breast tenderness and painful periods.
- Isotretinoin. Isotretinoin (Amnesteem, Claravis, others) is a derivative of vitamin A. It may be prescribed for people whose moderate or severe acne hasn't responded to other treatments.

MICROSPONGES DRUG DELIVERY SYSTEM

Microsponges are polymeric delivery systems composed of porous microspheres. They are tiny sponge- like spherical particles with a large porous surface. Moreover, they may enhance stability, reduce side effects and modify drug release favorably. Microsponge technology has many favorable characteristics, which make it a versatile drug delivery vehicle. Microsponge Systems are based on microscopic, polymer- based microspheres that can suspend or entrap a wide variety of substances, and can then be incorporated into a formulated product such as a gel, cream, liquid or powder. The outer surface is typically porous, allowing a sustained flow of substances out of the sphere. Microsponges are porous, polymeric microspheres that are used mostly for topical use and have recently been used for oral administration. Microsponges are designed to deliver a pharmaceutical active ingredient efficiently at the minimum dose and also to enhance stability, reduce side effects, and modify drug release.



Microsponges are patented polymeric delivery systems consisting of porous microspheres that can entrap a wide range of active ingredients such as emollients, fragrances, essential oils, sunscreens, and anti- infective, anti-fungal, and anti-inflammatory agents. Like a true sponge, each microsphere consists of a myriad of interconnecting voids within a non-collapsible structure, with a large porous surface. The microsponge technology was developed by Won in 1987, and the original patents were assigned to Advanced Polymer Systems, Inc. This company developed a large number of variations of the technique and applied those to the cosmetic as well as over-the-counter (OTC) and prescription pharmaceutical products. At the present time, this interesting technology has been licensed to Cardinal Health, Inc., for use in topical products. The size of the microsponges can be varied, usually from 5 – 300 µm in diameter, depending upon the degree of smoothness or after-feel required for the end formula. Although the microsponge size may vary, a typical 25 µm sphere can have up to 250000 pores and an internal pore structure equivalent to 10 ft in length, providing a total pore volume of about 1 ml/g. This results in a large reservoir within each microsponge, which can be loaded with up to its own weight of active agent. The microsponge particles themselves are too large to be absorbed into the skin and this adds a measure of safety to these microsponge materials. Another safety concern is the potential bacterial contamination of the materials entrapped in the microsponge. As the size of the pore diameter is smaller, the bacteria ranging from 0.007 to 0.2 µm cannot penetrate into the tunnel structure of the microsponges. (biharee a et.al.2023)

MATERIAL AND METHODS

Selection of drug and excipients

Table 1: Drug and excipients used

S. No.	Name of Chemicals
1	Nadifloxacin
2	Methanol
3	Ethanol
4	Acetonitrile
5	Ethyl cellulose
6	PVA
5.	Carbopol 934
6.	Triethanolamine
7.	Propylene glycol
8.	Methyl paraben

Pre-formulation studies

Organoleptic Properties

Organoleptic properties of Nadifloxacin were observed by visual observation. The organoleptic studies of Nadifloxacin like general appearance like color, odor, state, etc. were observed/ performed.

Solubility study

Qualitative solubility of Nadifloxacin in various solvents was measured using USP NF, 2007. Approximately 1 mg of Nadifloxacin was weighed and transferred into a 10 ml test tube and dissolved in the respective solvents (1 ml each of methanol, ethanol, PBS Solution, and water) (Jain and Verma 2020).

Melting Point

Melting point was analyzed by open Capillary method using Thiele's tube. Few quantity of the Nadifloxacin was placed in a thin walled capillary tube 10-15 mm long, about 1mm inside diameter,

and closed at one end. Liquid paraffin oil was filled in the thieles tube and placed in the contact of flame. The capillary was suspended into the Thiele's tube and heat the sample slowly; thermometer was attached to check the temperature. The temperature at which the sample starts to melt was taken as the melting point of the sample ((Chowk, M. I. 2020).

Determination of Lambda max and calibration curve

Lambda (λ) max

A stock standard solution containing 1 mg/mL of Nadifloxacin was prepared in methanol. Working standard solution equivalent to 100 µg/mL of Nadifloxacin was prepared by appropriate dilution of stock solution with the same solvent. The solution was scanned in the range of 200 – 400 nm UV spectrum using shimadzu 1700 double beam spectrophotometer (Kumbhar and Salunkhe 2013).

Standard calibration curve

100 mg of Nadifloxacin was accurately weighted into 100 ml volumetric flask, dissolved in Methanol and volume was made up with same solvent. Pipette 1ml of this solution into another 10 ml volumetric flask and the volume was made with Methanol and marked as Stock. The resultant solution is scanned in the range of (200-400 nm) by UV Spectrophotometer to get absorption maximum (λ max).

Preparation of calibration curve

The prepared stock solution was further diluted with solvent to get working standard solution of 2, 4, 6, 8, 10, 12 and 14 µg/ml of Nadifloxacin to construct Beer's law plot for the pure drug, the absorbance was measured, against solvent as blank. The standard graph was plotted using the drug concentration (X-axis) and absorbance (Y-axis) in the range of 2-14 µg/ml (Behera et al., 2012).

Fourier transmission Infra-Red Spectroscopy

FT-IR spectrum of Drug was recorded over the range of 4000 to 400 cm−1 by KBr pellet method using a FT-IR spectrophotometer. The KBr disc was prepared using 1 mg of each Drug in 100 mg of spectroscopic grade KBr which has been dried using IR lamp. Both KBr and drug was mixed and subjected to hydraulic pressure to form disc. This disc was placed in FT-IR chamber. Infrared spectrum was recorded in the 4000- 400 cm-1 region (Chowk M. I. 2020).

Formulation of Micro sponges

The micro sponges containing Nadifloxacin were fabricated by quasi-emulsion solvent diffusion method using an inner phase comprising Eudragit RS-100 and dibutyl phthalate (1%w/v) dissolved in 10 ml of ethanol: dichloromethane (1:1). Dibutyl phthalate was added to improve the plasticity of the polymer. Further Nadifloxacin was put in and dissolved through ultrasonication at 35°C. This mixture was then poured into an aqueous solution of PVA (outer phase) with stirring rate 500 rpm for 60 min. Next on, micro sponges were formed due to the removal of dichloromethane and ethanol from the system by evaporation. Prepared micro sponges were then filtered washed with distilled water and subjected to drying at 40°C for 12 h in hot air oven. Various formulation batches are prepared as per Table 1 (Bhatia et al., 2018, Moin et al., 2016).

Table 2 : Composition of formulation

S. No	Ingredients	MS 1	MS 2	MS 3	MS 4	MS 5
1.	Drug (Nadifloxacin) mg	100	100	100	100	100
2.	Eudragit RS 100 (mg)	100	200	300	400	500
3.	Poly vinyl alcohol (PVA) (%)	0.5	0.4	0.3	0.2	0.1
	Dibutyl phthalate (%)	1	1	1	1	1

4.	Ethanol: Dichloromethane(ml)(1:1)	10	10	10	10	10
5.	Distilled water (ml)	100	100	100	100	100
6.	Stirring time (min.)	60	60	60	60	60

Evaluation parameter of Micro sponges

Particle size

The particle size analysis of Nadifloxacin loaded Micro sponges was performed by using ‘‘Malvern Zetasizer (Malvern Instruments). The sample under investigation was diluted with distilled water (1: 200) and filled in disposable polystyrene cuvette. Measurement of particle size was done based on the dynamic light scattering (DLS) theory (Ahmed et al., 2021).

Zeta potential

The zeta potential was measured for the determination of the movement velocity of the particles in an electric field and the particle charge. In the present work, the Micro sponges was diluted 10 times with distilled water and analyzed by Zetasizer Malvern instruments. All samples were sonicated for 5-10 minutes before zeta potential measurements (Kumar et al., 2018, Penjuri et al., 2016).

Entrapment efficiency

To calculate the entrapment efficiency accurately weighed the quantity of Micro sponges (100 mg) with 5 ml of PBS solution 7.4 in a volumetric flask was shaken for 1 min using vortex mixer. The volume was made up to 10 ml. Then the solution was filtered and diluted and the concentration of entrapped Nadifloxacin was determined spectrophotometrically (Solunke et al., 2019).

%EE = Initial amount of drug added - Drug amount in supernatant / Initial amount of drug added * 100

Scanning Electron Microscopic (SEM)

The electron beam from a scanning electron microscope was used to attain the morphological features of the Nadifloxacin loaded Micro sponges were coated with a thin layer (2–20 nm) of metal(s) such as gold, palladium, or platinum using a sputter coater under vacuum. The pretreatment specimen was then attacked with an electron beam, which resulted in the creation of secondary electrons known as augers. From this interaction between the electron beam and the specimen's atoms, only the electrons dispersed at 90° were picked and further processed based on Rutherford and Kramer's Law to obtain images of surface topography (Anwer et al., 2019)..

Formulation of Micro sponges loaded Gel

Initially, carbopol-934 was immersed in 50 mL of warm water (A) for 2 hours and homogeneously distributed using a magnetic stirrer at 600 rpm. In a separate container, carboxymethyl cellulose and methyl paraben were mixed with 50 ml of warm water (B) and agitated continuously to form a hard gel. Both mixes A and B were stirred continuously. Then tri-ethanol amine (Drop wise) was added to neutralize the pH and Micro sponges of optimized formulation were incorporated into the dispersion to obtained Gel. At this stage, permeation enhancer (Propylene glycol) was added. The final dispersion was agitated until smooth gel was formed without lumps (Abbas et al., 2019, Silpa et al., 2021)..

Table 3: Composition of gel formulation

S. No	Excipients	Quantity (gm)
1.	Carbopol 934	1.00 gm
2.	Carboxymethyl cellulose	1.00 gm
3.	Propylene glycol	0.5 ml
4.	Methyl paraben	0.2 ml

5.	Micro sponges	1.0 gm
6.	Tri-ethanolamine	q.s
7.	Water	100 ml

Characterization of Micro sponges loaded Gel

Physical appearance

The prepared Gel formulation was evaluated for appearance, Color, Odor, and homogeneity by visual observation (Kumar and Eswaraiah 2020).

pH Determination

pH of the formulation was determined by using Digital pH meter (EI). The meter was allowed to stabilize as needed before being calibrated. Rinse the probe with de-ionized or distilled water and blot it dry with lint-free tissue paper. Immerse the sensor tip of the probe in the sample and record the pH reading. Rinse the probe, blot it dry, and repeat step 2 with a fresh sample. The two readings should agree to within the accuracy limits of the meter. The samples were examined in triplicate. If tiny differences in pH were noticed, it was corrected to skin pH by adding tri-ethanolamine solution drop by drop (Monica and Gautami 2014).

Viscosity

The viscosity of the gel formulations was determined using Brookfield viscometer with spindle no. 61 at 100 rpm at the temperature of 250C.83

Spreadability

An ideal topical gel should have a high spreading coefficient when applied or rubbed over the skin's surface. This was assessed by placing approximately 1g of formulation on a glass slide. Another glass slide of the same length was placed above that, and a mass of 50 mg was put on the glass slide so that the gel gets sandwiched between the two glass slides and spreads at a certain distance. The time taken for the gel to travel the distance from the place of its position was noted down. Spreadability was determined by the following formula

$$S= M*L/T$$

Where, S-Spreadability, g.cm/s M-Weight put on the upper glass L-Length of glass slide T-Time for spreading gel in sec (Sandeep, D. S. 2020).

In-vitro drug release study

The in-vitro drug release study of Nadifloxacin loaded Micro sponges gel formulation was studied by dialysis bag diffusion method. Nadifloxacin loaded Micro sponges gel were dispersed into dialysis bag and the dialysis bag was then kept in a beaker containing 100 ml of pH 7.4 phosphate buffer. The beaker was placed over a magnetic stirrer and the temperature of the assembly was maintained at 37 ± 2 °C throughout the experiment. During the experiment rpm was maintained at 100 rpm. Samples (2 ml) were withdrawn at a definite time intervals and replaced with equal amounts of fresh pH 7.4 phosphate buffers. After suitable dilutions the samples were analyzed using UV–Visible spectrophotometer. To analyze the in vitro drug release data various kinetic models were used to describe the release kinetics.

Well Diffusion Assay

The bacterial suspension of E. coli was standardized to 108 CFU/ml of bacteria and kept into the shaker. Then, 100µl of the inoculums from the broth (containing 108 CFU/ml) was taken with a micropipette and then transferred to fresh and sterile solidified Agar Media Plate (Mohammadi et al., 2012). The agar plate was inoculated by spreading the inoculums with a sterile spreader, over the entire sterile agar surface. Three wells of 6 mm were bored in the inoculated media with the help of sterile cork-borer. The wells were then formed for the inoculation of the micro sponges loaded Gel (1mg/ml) and (0.5mg/ml) solution. 100 µl of the sample was loaded. It was allowed to diffuse for about 30 minutes at room temperature

and incubated for 18-24 hours at 37o C. After incubation, plates were observed for the formation of a clear zone around the well which corresponds to the antimicrobial activity of tested compounds. The zone of inhibition (ZOI) was observed and measured in mm. Zones were measured to a nearest millimeter using a ruler, which was held on the back of the inverted Petri plate. The Petri plate was held a few inches above a black, non-reflecting background. The diameters of the zone of complete inhibition (as judge by unaided eye) were measured, including the diameter of the well.

Stability study

The micro sponges loaded gel formulation was packed and were placed in the stability test chamber and subjected to stability studies at accelerated testing (250C±20C and 60 ± 5% RH) and (400C±20C and 70 ±5% RH) for 3 months. The formulations were checked for evaluation parameter viscosity and pH studies at the interval of 30, 45, 60, 90 days (3 month) months. The formulation was tested for stability under accelerated storage condition for 3 months in accordance to International Conference on Harmonization (ICH) guidelines. Formulation was analyzed for the change in evaluation parameter viscosity and pH studies (Sharma et al., 2011). All Results were compared against final formulation of 0 days as the reference.

RESULT AND DISCUSSION

Pre-formulation study of drug

Table 4.: Organoleptic properties of Nadifloxacin

Drug	Organoleptic properties	Observation
Nadifloxacin	Color	White
	Odor	Odorless
	Appearance	Powder
	State	Solid powder

An evaluation of the API's organoleptic qualities, including Appearance, color, odor, and state, was conducted. Nadifloxacin was FOUND to have a white color to it when tested. Nadifloxacin has an odorless and has a solid state powder form,

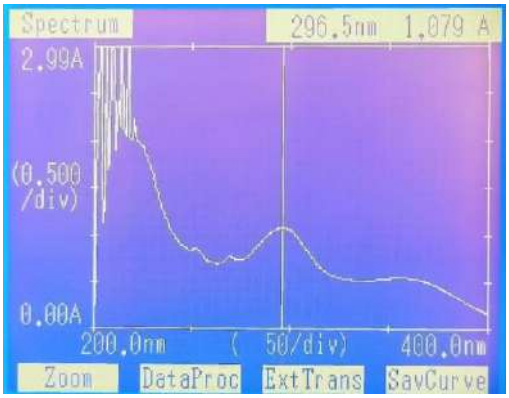
Solubility study

Table 5.: Solubility study of Nadifloxacin

Drug	Solvents	Observation/Inference
Nadifloxacin	Water	Slightly Soluble
	Ethanol	Slightly soluble
	Methanol	Soluble
	PBS 7.4	Freely Soluble
	DMSO	Freely soluble

The solubility of Nadifloxacin was determined in various non-volatile or volatile liquid vehicles such as Dimethyl sulfoxide, methanol, ethanol, PBS solution, and water shown in . From the results, it was observed that the drug is freely solu'ble in Dimethyl sulfoxide and PBS solution and soluble in methanol. The capillary method is used to determine the melting point of a substance. The melting point of the Nadifloxacin was found to be 247ºC, which is well within the limits of the drug specification The digital pH meter used to determine the pH of a substance. The pH of the Nadifloxacin was found to be 7.2, which is well within the limits of the drug specification. Lambda max- Double beam UV visible spectrophotometer (Shimadzu- 1700) was used to determine the

lambda max (absorption maxima) of a substance. The lambda max of the Nadifloxacin was found to be 296.0 nm. This is well within the limits of the drug specification



Calibration curve of Nadifloxacin-

The linearity of the proposed method was established by least squares linear regression analysis of the calibration curve. The regression equation for Nadifloxacin was obtained by plotting absorbance versus concentration of Nadifloxacin in the range of 2-14 µg/mL. Seven points calibration curve were obtained in a concentration range from 40-100 µg/ml for drug. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.0496x + 0.062 with correlation coefficient R^2 = 0.973.

Table.6: Calibration curve

Concentration (µg/ml)	Absorbance (296.0 nm)
0	0
2	0.187
4	0.298
6	0.308
8	0.423
10	0.540
12	0.663
14	0.792
Mean	0.458714286
SD	0.217204753
%RSD	47.37

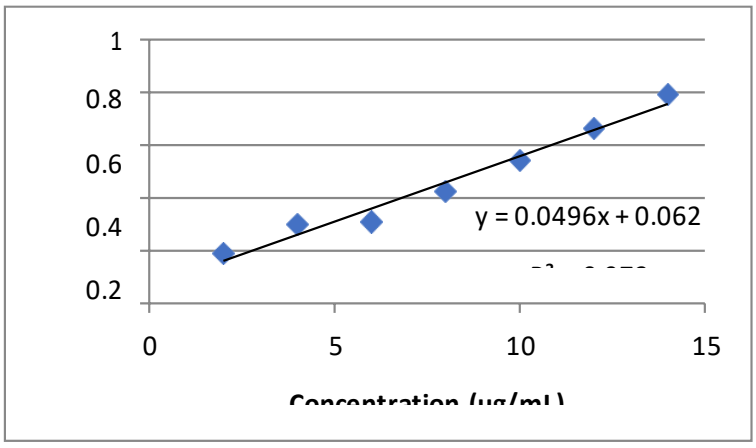


Figure 4 : Calibration curve of Nadifloxacin

Characterization of micro sponges-

Particle size –

The particle size is one of the most important parameter for the characterization of micro sponges. The average particle size of the prepared drug loaded micro sponges was measured using Malvern zeta sizer. Particle size analysis showed that the average particle size of drug loaded micro sponges was found to be range 498.5 nm to 750.2 nm.

Table 7: Particle size

S. No	Formulation code	Particle size (nm)
1.	Micro sponges M1	687.1nm
2.	Micro sponges M2	498.5 nm
3.	Micro sponges M3	575.9 nm
4.	Micro sponges M4	644.2 nm
5.	Micro sponges M5	750.2 nm

Zeta potential-

analysis is carried out to find the surface charge of the particles to know its stability during storage. The magnitude of zeta potential is predictive of the colloidal stability. If the particles in micro sponges have a large positive zeta potential then they will tend to repel each other and there will be no tendency for the particles to come together. However, if the particles have low zeta potential values then there will be no force to prevent the particles coming together and flocculating for micro sponges. Zeta potential of all formulations was found to be range -0.9 mV to -4.1 mV with peak area of 100% intensity. These values indicate that the formulated micro sponges

Table8: Zeta potential

S. No	Formulation Code	Zeta potential
1.	Micro sponges M1	-0.9 mV
2.	Micro sponges M2	-2.3 mV
3.	Micro sponges M3	-4.1 mV
4.	Micro sponges M4	-2.9 mV
5	Micro sponges M5	-3.7 mV

Entrapment efficacy-

This might be due to the fact that the variation in entrapment efficiency was due to the changes in the polymer concentration and difference in the degree of cross linking. The prepared micro sponges possess drug entrapment range (70.20 to 91.09). The F2 micro sponges possess high drug entrapment efficiency and were found to be in the range of 91.09%.

Table.9: Entrapment efficacy

S. No.	Formulations (M1-M5)	Entrapment efficacy (%)
1.	Micro sponges M1	89.39
2.	Micro sponges M2	91.09
3.	Micro sponges M3	86.32
4.	Micro sponges M4	78.81
5.	Micro sponges M5	70.20

Scanning electron microscope (SEM) of F2 Formulation (Optimized- SEM analysis was performed to determine their microscopic characters (shape & morphology) of prepared micro sponges. Micro sponges were prepared and dried well to remove the moisture content and images were taken using scanning electron microscopy. Scanning electron micrograph of the prepared micro sponges at 23.41 KX magnification showed that the micro sponges were porous with a smooth surface morphology and spherical shape. The spongy and porous nature of micro sponges was clearly observed in the SEM images.

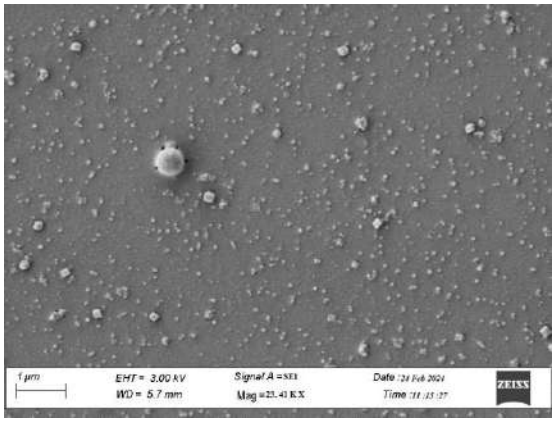


Figure 5 Scanning electron microscope

Characterization of micro sponges loaded gel

Physical appearance-

An evaluation of the gel, including color, odor, appearance and homogeneity, was conducted. Gel was discovered to have a brownish color to it when tested. Gel does not have a distinctive odor and has a transparent appearance, according to research conducted on it.

Viscosity of Gel -The viscosity was measured by the Brookfield viscometer spindle no. 61 at 100rpm. The result was shown in the table 13. The viscosity of Gel was found to be 6854 centipoise respectively.

pH determination-

The pH of the gel formulation was found to be 6.9, which lies in the normal pH range of the skin and would not produce any skin irritation. There was no significant change in pH values as a function of time. The physicochemical properties of prepared gel formulation were in good agreement.

Spreadability-

One of the essential criteria for a Gel is that it should possess good spreadability. Spreadability depends on the viscosity of the formulation and physical characteristics of the polymers used in the formulation. A more viscous formulation would have poor spreadability. Spreadability is a term expressed to denote the extent of area on which the gel readily spreads on application to the skin. The therapeutic efficacy of a formulation also depends upon its spreading value. The spreadability of Gel formulation is found to be

Table10: Antimicrobial activity of gel against E.coli

Time(Hr)	cumulative %drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released
0	0	100	0.000	2.000	0.000	0.000
1	15.12	84.88	1.000	1.929	0.000	1.180
2	36.45	63.55	1.414	1.803	0.301	1.562
3	43.77	56.23	1.732	1.750	0.477	1.641
4	57.14	42.86	2.000	1.632	0.602	1.757
5	66.32	33.68	2.236	1.527	0.699	1.822
6	77.2	22.8	2.449	1.358	0.778	1.888
7	82.75	17.25	2.646	1.237	0.845	1.918

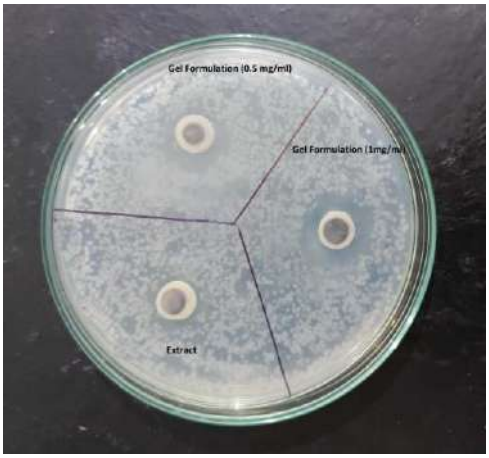


Figure 6: Antimicrobial activity against E. coli

Stability study

Formulation were found to be stable, both physically and chemically, for a period of 3 months at accelerated stability conditions (250C±2 0C and 60 ± 5% RH) and (400C±2 0C and 70 ±5% RH). Evaluation parameters including viscosity and pH studies were not altered significantly. Results of assay and other evaluation criteria at periodic time points of stability studies are summarized in Table The result of accelerated stability studies of micro sponges formulation is Show in above table no major changes were observed.

Table 11 : Stability Study of optimized formulation (micro sponges gel)

S. No	Time (Days)	25^0C±2 ^{0}C and 60 ± 5% RH		40^0C±2 ^{0}C and 70 ±5% RH	
		Viscosity	pH	Viscosity	pH
1.	0	6854	7.2	6854	7.2
2.	30	6840	7.7	6839	7.4
3.	45	6842	7.1	6843	7.1
3.	60	6844	7.1	6849	7.4
4.	90	6849	7.3	6851	7.6

SUMMAARY AND CONCLUSION

Nadifloxacin was discovered to have a white color to it when tested. Nadifloxacin has an odorless and has a solid state powder form, according to research conducted on it. The melting point of the Nadifloxacin was found to be 247ºC and the pH of the Nadifloxacin was found to be 7.2, which is well within the limits of the drug specification. The lambda max of the Nadifloxacin was found to be 296.0 nm. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.0496x + 0.062 with correlation coefficient R^2 = 0.973. Formulation was carried out by quasi-emulsion solvent diffusion method. Trial batches indicated that polymers are suitable for the Nadifloxacin loaded micro sponges gel formulation. Eudragit RS 100 and Poly vinyl alcohol were selected for further studies. Scanning electron micrograph of the prepared micro sponges at 23.42 KX magnification showed that the micro sponges were porous with a smooth surface morphology and spherical shape. The spongy and porous nature of micro sponges was clearly observed in the SEM images. Particle size and zeta potential was determined by Malvern Zeta sizer. The particle size analysis confirmed that the prepared sample were in the nanometer range. Average particle size obtained for the formulations F1 and F5 were 498.5 nm to 750.2 nm. Zeta potential values of micro sponges indicated that the formulated micro sponges are stable. The amount of drug being entrapped in micro sponges was calculated and all the prepared micro sponges were found to possess very high entrapment efficiency. The viscosity of micro sponges loaded gel is found to 6854±0.34cps. The ph of microsphere loaded gel is 6.4 and spreadability is 12.97, indicating that micro sponges loaded gel has high release and permeability. Therefore, in this study Nadifloxacin loaded in micro sponges to improve solubility and bioavailability. So this can be overcome by

developing nanotechnology based formulation like micro sponges which may increase the bioavailability. Through the different evaluation parameters the formation of micro sponges confirmed and via drug release study as well as solubility study proven the enhancement of the bioavailability of the drug. The discovery of micro sponges has become a significant step in overcoming certain problems such as drug toxicity, poor bioavailability and release of drug in a predictable fashion as they can accommodate both hydrophilic and hydrophobic drug. Micro sponges exhibit a porous structure in nature which has the unique ability to entrap the drug moieties and offers a merit of desire release. The formulated Nadifloxacin containing micro sponges loaded gel can be used in the treatment of various skin diseases. This can be targeted to the skin cells and produce sustained drug delivery which in turn reduces the dose, frequency of administration and the side effects.

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