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Research Article of Formulation & Evaluation of Nitrofurantoin Nanogels

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ABSTRACT:
This comprehensive study focuses on the meticulous development and through characterization of nitrofurantoin-loaded nanogels, aiming to significantly improve antimicrobial efficacy and therapeutic outcomes. Nanogels were meticulously formulated using an optimized polymeric matrix and further refined using a design to ensure precision and consistency. The prepared nanogels exhibited a desirable particle size range of 150-250 nm, with remarkably high encapsulation efficiency (>80%) and sustained in vitro drug release profiles, indicating potential for prolonged therapeutic action. Moreover, the nanogels demonstrated notably enhanced antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus* compared to pure nitrofurantoin, underscoring their promise in combating resistant microbial strains. The results suggest that nitrofurantoin- loaded nanogels could be a ground breaking approach for targeted and controlled delivery of antibiotics, potentially improving treatment outcomes for urinary tract infections and reducing the risk of antibiotic resistance.

INTRODUCTION:
Recent advancements in high throughput screening and drug manufacturing have directed drug research and discovery towards lipophilic pharmacological moieties. At the moment, about 40% of pharmaceuticals on the market and 90% of medications in the development pipeline are lipophilic[1]. The lipophilic nature of the medications causes issues with low solubility, erratic absorption and pharmacokinetic heterogeneity between and within subjects. To make active moieties more soluble, a variety of methods have been used. These methods include complexation, amorphization and decrease of particle size, and Nano carrier drug delivery systems in addition to physical and chemical alteration of the API[2].
Even with the use of several technologies to increase the solubility, oral medication delivery is not always practical due to the drugs' low bioavailability, which is link in to poor absorption, first-pass metabolism, and chemical and enzymatic degradation[2,3]. Oral medicine distribution is further complicated by clinical problems and low drug concentrations at the site of action. For instance, the oral administration of disease- modifying anti-rheumatic medications (DMARDs), which are used to treat arthritis, has been linked to a number of adverse consequences, including hepatotoxicity, hematologic toxicity, and carcinogenicity[4,5]. By using the medication topically, these clinical problems can be reduced[5]. Since the skin is the body's first line of defense when it comes to topical distribution, it views the APIs as foreign substances and prevents them from entering the body. The stratum corneum, the outermost layer of the epidermis, is the first and hardest layer to penetrate in order for a medication to enter the skin[6]. Numerous

methods have been investigated to improve the drug's penetration. One such process is the disturbance of the structure of the skin layer, which can be accomplished by means of methods like electroporation, chemical penetration enhancers, ultrasound, iontophoresis, and sonophoresis[7].On the other hand, it has been found that using nano-carriers to get over the SC barrier and achieve effective drug penetration can do so without aggravating skin injury. They use intra- and intercellular transport mechanisms to help distribute drugs through the skin, engaging with skin constituents to mediate transport or form drug depots for sustained or stimulus-induced release.

These innovative topical lipid carriers comprise, but are not restricted to, liposomes, micelles, dendrimers, solid lipid nanoparticles, emulsions (nano/micro), and nano-structured lipid carriers[8,9]. Since they are stable, easy to manufacture, have excellent drug-loading and solubilizing capacities, and have regulated release patterns, nano-emulsions are among the candidates for drug delivery systems. In comparison to liposomes, these nano-emulsions lipophilic core permits the passage of more lipophilic molecules across topical membranes[10,11]. Furthermore, the instability of liposomes has always been a problem since they break down throughout the penetration process. Similarly, solid-lipid nanoparticles' poor drug loading capacity and uncontrolled release make them unsuitable for cutaneous drug administration. Micelles also show inadequate encapsulation efficiency and stability. Similarly, dendrimers' poor regulated release behavior and toxicity restrict the risen topical medicine[11].

Hetero generous colloidal mixes of water and oil, one in a continuous phase and the other as a dispersed phase, are known as nano-emulsions. At the interface between the dispersed and continuous phases, a surfactant known as an emulsifier is adsorbed, reducing the surface tension and stabilizing the system. Comparing these systems to simple emulsions like micelles, suspensions, etc., they have a longer shelf life due to their great thermodynamic stability. Nano-emulsions have several benefits, but their low viscosity, which results in a short retention period and poor Spreadibility, limits them. By converting the nano-emulsion into a nano-emulgel and employing an appropriate gelling agent, these issues can be fixed[12,13].

The nano-emulgel, which is a blend of gel and emulsion, functions as a colloidal system. The emulsion component enhances penetration like other nano-carriers while shielding the medication from hydrolysis and enzymatic destruction. Maintaining the drug's therapeutic concentrations for an adequate amount of time is just as critical as increasing the drug's penetration through the skin. In addition to lowering surface and interfacial tension and increasing retention duration through enhanced Spreadibility and viscosity, the gel component also increases thermodynamic stability. When compared to other nano-carriers, nano-emulgel has a number of advantages, including a high drug loading capacity, improved penetration, diffusion, and little skin irritation [14,15].

Drug Delivery through a Topical Route

Any perfect formulation should have superior pharmacological activity, less side effects, self-administration, patient compliance, and non-invasiveness. The majority of the previously listed features are present in the topical route delivering formulations[16]. Avoiding the hepatic first-pass effect, less adverse effects because of the local site of action, improved percutaneous absorption, and topical application that may even raise bioavailability with a prolonged deposition are some advantages of the topical route of administration[17]. Other benefits include the capacity to precisely target the medicine at the intended place and a decrease in drug loss via metabolism or breakdown. A combination of minimizing drug breakdown and continuously administering the medicine over an extended period of time causes the drug to prominently pass the stratum corneum barrier, improving bioavailability[18,19].

Numerous studies have demonstrated an improvement in the bioavailability of medications when applied topically. For instance, topical application of flurbiprofen nano-emulsion increased its bioavailability by 4.4 times when compared to oral delivery [20]. When compared to an emulsion formulation, Zhouetal's nano-emulsion of nil red dye showed a ten-fold improvement in dye penetration into the skin[21]. Another study found that employing micro-emulsions for transdermal delivery increased Lacidipine bioavailability by 3.5 times. According to the group, this improvement might be the result of the medication's first-pass

effect being avoided when applied topically [19,22]. Furthermore, topical preparations of therapeutically active drugs have been shown to boost their pharmacological and therapeutic effects.

Topical formulations that are commonly utilized include gels, patches, ointments, lotions, creams, and solutions[23]. However, as Figure 1.1 illustrates, these topical treatments must pass through the skin's live epidermis as well as the extraordinarily efficient and capable stratum corneum barrier. The SC presents a significant obstacle to the topical or transdermal distribution of therapeutically active drugs sinceitisa10–20 µm thick lipid-inter aspersed matrix of terminally developed keratinocytes[24-26] lowering the quantity of medication that reaches the intended location.

The topical medicines that are sold exhibit low penetration, which results in a subpar therapeutic impact[27,28]. Thus, the creation of topical formulations with suitable permeability and guaranteeing administration by several path ways is the primary focus of research in this field. Recent years have seen a shift in research focus towards innovative carrier systems with the goal of changing how permeable hydrophobic medications are through the skin. Recent years have seen the emergence of new formulation development processes and tactics; nevertheless, the primary disadvantage of these approaches is the use of chemicals and non-green solvents to increase penetration. Long-term use of these preparations could result in a number of skin issues[28,29]. In addition to the different constraint that the skin presents, an active moiety needs to have specific qualities in order to be appropriate for the topical delivery route, as shown in table 1.1[30,31].

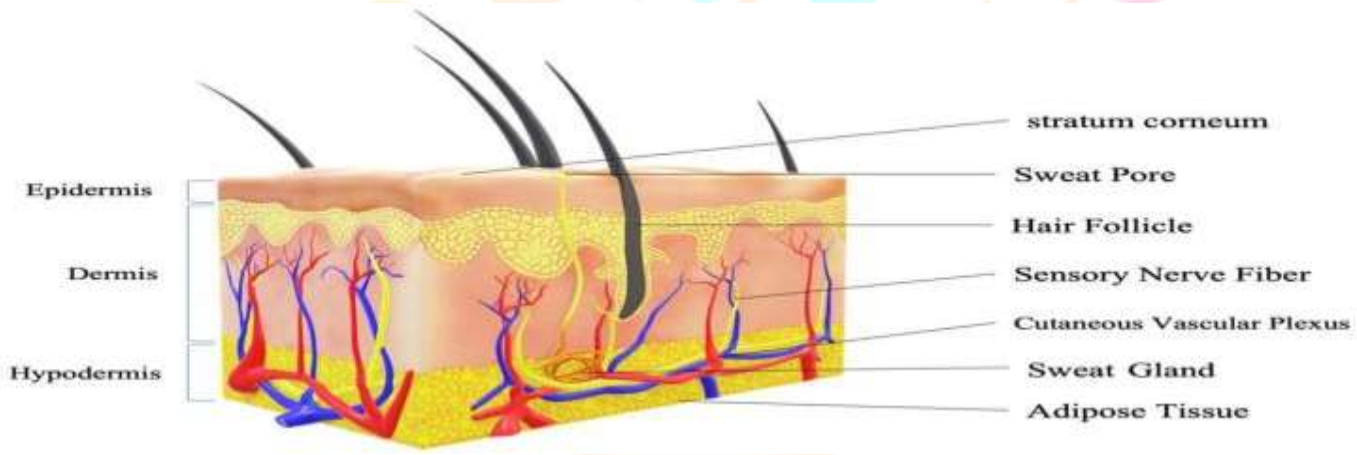


Figure 1.1 Morphology of human skin.

Table 1.1 Primary requirement of active moiety for topical delivery.

Properties	**Conditions**
t1/2	≤10 h
Molecular mass	≤500 Daltons The limit can be exceeded by altering the permeability of skin
Molecular size	Small
Polarity	Non-polar is desirable
Log P	0.8–5
pKa	Higher
Irritation on skin	Non-irritating
Skin Permeability coefficient	≥0.5×10^{-3}cm/h

Nano Emulsions in Topical Delivery

Lipid-based nano-formulations are the result of advancements and innovations in topical and transdermal medication delivery methods. Despite the fact that there are several forms, research on nano-emulsions has advanced because of the previously described benefits and their capacity to administer hydrophobic medications in a non- invasive manner without the need for a penetration enhancer [32]. An isotropic

biphasic combination of two components, water and oil, in which one phase is distributed as nanoscale droplets in the other, is called a nano-emulsion. The application of a surfactant interfacial layer stabilizes the system[33]. The lowered tendency of nano- emulsions to experience phase's parathion sets them apart from conventional emulsions[34]. Numerous in-vivo investigations have been conducted to validate the potential uses and viability of topical micro- and nano-emulsions. Additionally, in-vitro studies have backed the application of the set topical lipidic compositions[35]. These systems of nano- emulsions appear transparent or translucent. Compared to other lipid carriers, nano- emulsions have a higher thermodynamic stability. When it comes to solubilization capacity, nano-emulsions outperform solutions of simple micelles[36].

Because of the oil droplets' nanoscale and enhanced surface area, these formulations have the ability to solubilize and incorporate significant amounts of active pharmacologicalmolecules[37, 38]. The common problems in an emulsion are the phenomena of creaming or sedimentation. Because of Brownian motion and the reduced gravitational force exerted on the particles due to their nano size, a nano-emulsion's stability is enhanced and stability problems likewise dimentation and creaming are avoided[38]. Several studies have shown that when medications are provided as nano-emulsion systems, they penetrate the body more deeply than when they are administered in conventional formulations such as emulsions, creams, and ointment gels[37-39]. Due to the nano-emulsion's capacity to break through the firmly bonded lipid bi-layers, it is able to penetrate deeply in to the skin and deliver the drug to the systemic circulation. Additionally, the smaller dispersed droplets facilitate both trans-cellular and para-cellular transport[13].

Nano-Emulgel Drug Delivery System

Nano-emulsions have several benefits, however because of their low viscosity, they are not easily dispersed and do not retain the formulation well on the skin[40]. This restriction makes it difficult to use nano-emulsions in clinical settings[41]. By adding a gelling agent to the nano-emulsion and creating a nano-emulgel, this problem has been fixed[42]. To make gels, massive amounts of aqueous or hydro alcoholic bases are used in a colloidal particle environment[43]. By combining the nano-emulsion with a hydro gel matrix, nano- emulgel is created, therefore lowering the emulsion's thermodynamic instability. Because of the external medium's greater consistency, the non-aqueous phase's mobility has decreased, leading to an improvement in thermodynamic stability. For topical administration, nano-emulgel is a controlled release dosage form that benefits medications with a short half-life because of its improved retention time and thermodynamic stability, which allow the drug to be released gradually [14,44]. The drawbacks of both separate methods are eliminated when nano-emulsion is added to a gelling system. The resulting nano-emulgel combines the sophisticated qualities of a nano-emulsion with the gel-like qualities of a gel. Because of its smaller particle size and thermodynamic stability, nano-emulgel has advantages over conventional emulgel.

Enhancement of epidermal penetration, increased loading of an active moiety, reduced irritation, and increased spreadability are among the many advantages provided by nano-emulgels. This becomes clear when contrasting it with other nano-carriers such liposomes and solid lipid nanoparticles. The gel's higher viscosity renders the nano-emulsion appropriate for topical usage. To achieve the same, various gelling agents compatible with skin like xanthan gum, carbomer 980, Pluronic's, carrageenan, and carbomer 934 are used for topical application[14,45]. In nano-emulsions, acceptable localization and medication dispersion are accomplished through sufficient percutaneous absorption through the skin. Through the skin, this aids in boosting the efficacy both locally and comprehensively. Drugs can also be administered to the central nervous system (CNS) using this approaches since it can pass past the blood-brain barrier when injected via the nasal route[46]. Better patient compliance is made possible by the non-greasy and non-irritating properties of nano- emulgel[43]. These systems also have the added benefit of having pharmacokinetic qualities including improved absorption and fewer side effects [47]. The hydro gel matrix, uniformity, and consistency have contributed to the increased attention being paid to nano-emulgels. Additionally, a number of studies have demonstrated that the reduced mobility of oil globules in the gel matrix of nano-emulgel results in less Oswalt ripening and greater stability[48]. Kaur et al., for example, created a topical

nano-emulgel that was loaded with TPGS that contained mefenamic acid. The optimised nano-emulgel demonstrated increased analgesic efficacy in the pharma co-dynamic investigation by enhancing % reaction time and inhibiting inflammation. When it came to medication penetration and long-term stability, the prepared nano-emulgel fared better than other conventional topical formulations[49].

Other than these, there are no other formulation stability constraints with nano-emulgel, such as the de stabilization issue with conventional emulgels, the moisture entrapment issue with powders, the cake formation issue with suspensions, the coalescence issue with oil globules, the formation of agglomerates in suspensions, and the poor adherence and excessive spreadability issue with nano-emulsions[43]. These reasons contribute to the widespread belief that nano-emulgel is a superior and unique topical medication delivery method compared to commercially available standard dosage forms. This new formulation is encouraging for studies aimed at different skin conditions and illnesses. In the topical delivery category, nano-emulgel is poised to become a popular alternative to conventional forms.

Urinary tract infections (UTIs)

Urinary tract infections, or UTIs, are among the most prevalent bacterial illness seen in clinical settings, impacting people of all ages and socioeconomic backgrounds globally. A variety of microbial diseases affecting the kidneys, ureters, bladder, and urethra are included in the category of urinary tract infections, or UTIs. Although the site of infection and the existence of complicating factors, such as an atomically anomalies or underlying medical disorders, are usually used to classify UTIs, pathogenic bacteria—*Escherichia coli* being the most common culprit—is the primary cause of UTIs. Varying populations experience UTIs at varying rates; women, young children, the elderly, and people with weakened immune systems are among the categories most at risk. Because of anatomical characteristics that favor the ascent of germs into the urinary tract, such as a shorter urethra and the urethral opening's closeness to the anus, women are more vulnerable to UTIs. Furthermore, hormonal fluctuations, like those that take place during menopause or pregnancy, might modify the micro biota in the vagina and make women more susceptible to recurring UTIs.

Depending on the location and intensity of the infection, UTIs can present with a broad spectrum of clinical symptoms. While fever, flank pain, nausea, and vomiting are common sign so upper UTIs (pyelonephritis), dysuria, frequency, urgency, suprapubic discomfort, and hematuria are common signs of lower UTIs (cystitis). When UTIs are severe, they can cause consequences like sepsis, bacteremia, renal abscess, and renal failure. This is especially true for people with impaired immune systems or those who have underlying urinary tract abnormalities. A combination of clinical evaluation, urinalysis, and microbiological culture of urine samples is usually used to diagnose UTIs. Pee culture finds the pathogen causing the infection and directs anti biotic therapy, whereas pee urinalysis helps detect leukocyte esterase, nitrites, and pyuria, all of which are indicative of bacterial infection. Insinuations of complex UTIs, imaging procedures like computed tomography (CT) or ultrasound may be required to check for structural abnormalities or consequences.

Antimicrobial therapy is the mainstay of UTI management; its goals are to eradicate the causing bacteria and reduce symptoms. Based on the clinical presentation and local epidemiological data, empirical antibiotic treatment is frequently started. Changes are made in response to urine culture and sensitivity results. A number of criteria, including the suspected pathogen, patterns of antibiotic susceptibility, the patient's features, and the existence of aggravating conditions, influence the choice of antibiotic therapy.
The growing incidence of antibiotic resistance in uro pathogens has been a substantial obstacle to the efficient treatment of UTI sin recent times. The increasing prevalence of multidrug-resistant bacteria, such as Enterobacteriaceae that produce extended- spectrum beta-lactamase (ESBL) and organisms resistant to carbapenems, has made the prudent use of antibiotics and the investigation of alternative treatment approaches necessary. Prevent interventions are essential in lowering the incidence of UTIs and avoiding recurring infections, even in the absence of antimicrobial therapy. UTI risk can be reduced by following good hygiene habits, such as enough hydration, voiding technique, and correct perineal care. Furthermore, for some people, behavioral changes including abstaining from substances that irritate the urinary system (such alcohol and caffeine) and engaging in safe sexual behavior may be helpful. Assuming all goes well;

UTIs pose a serious threat to public health due to the high morbidity and expense of treating and diagnosing them. Healthcare professionals must possess a thorough awareness of the epidemiology, clinical presentation, diagnosis, and management of urinary tract infections (UTIs) in order to offer patients with the best care possible. To further address the changing issues faced by UTIs in modern health care settings, initiatives to promote antimicrobials stewardship, prevent antibiotic resistance, and develop alternate treatment methods are essential.

Advanced UTI Treatment:

Harnessing the Potential of Nano-emulsion Gels With several advantages over conventional formulations, nano-emulsion gels represent and promising method in the treatment and management of urinary tract infections (UTIs). Uncommon and frequently repeated, UTIs are mostly caused by bacterial infections like *Escherichia coli* and can result in severe morbidity and health care costs if ignored or improperly managed. The development of nano-emulsion gels, which combine natural gums with antibacterial drugs like nitrofurantoin, has enormous potential to improve therapeutic outcomes and address the problems related to treating urinary tract infections.

The capacity of nano-emulsion gels to transport drugs to the urinary system in a sustained and targeted manner is one of their main benefits for managing urinary tract infections. The antibacterial agent can be more easily encapsulated thanks to the nano-emulsion formulation, which also increases the drug's solubility, stability, and bioavailability. By adding natural gums to the gel matrix, the formulation's muco adhesive qualities are further improved, encouraging extended contact with the uro epithelial surfaces and enhancing medication retention in the urinary system. By increasing the concentration of the medication at the infection site and minimizing systemic exposure and potential side effects, this targeted drug delivery strategy maximizes therapeutic efficacy.

Furthermore, when compared to traditional dose forms, nano-emulsion gels provide better tissue penetration and permeation, allowing for deeper penetration into the mucosal membranes and biofilms linked to UTIs. Bacterial aggregation covered in an extracellular matrix is known as biofilms, and they are important in the pathophysiology of urinary tract infections (UTIs) as well as treatment failure and antibiotic resistance. Because of their tiny droplet size and high surface area-to-volume ratio, nano emulsion gels are able to break through biofilms with effectiveness, making bacterial pathogens more susceptible to antimicrobial drugs and leading to better treatment outcomes. Furthermore, nano-emulsion gels offer formulation designers flexibility by enabling the addition of various adjuvant and therapeutic drugs to address various facets of UTI pathogenesis. To relieve UTI symptoms including pain, inflammation, and dysuria, nano emulsion gels canals be made with anti-inflammatory drugs, analgesics, and probiotics in addition to antibacterial compounds. Additionally, the formulation's use of natural gums supports the idea of holistic care, which emphasises the integration of sustainable and natural components to support general health and wellbeing.

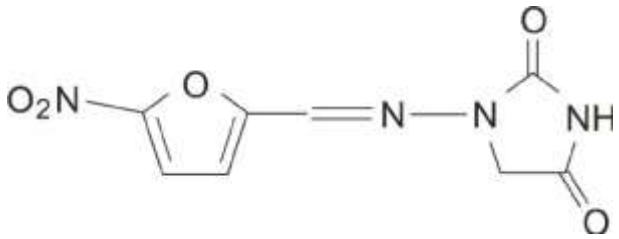
The ability of nano emulsion gels to address the problems caused by antibiotic resistance is a key benefit in the treatment of UTIs. Alternative therapeutic techniques that can successfully fight resistant bacteria and avoid treatment failure are desperately needed, as multidrug-resistant uropathogens are becoming more common. By delivering high concentrations of anti-microbial drugs directly to the site of infection, nano-emulsion gels can help combat bacterial resistance mechanisms and increase the effectiveness of antimicrobial therapy for urinary tract infections. It is assumed that nano-emulsion gels, with their targeted drug delivery, improved tissue penetration, formulation design diversity, and potential to overcome antibiotic resistance, hold considerable promise in the treatment and management of urinary tract infections. Through the utilization of the distinct characteristics of nano-emulsion systems and natural gums, these inventive formulations possess the capability to transform the management of urinary tract infections, enhance patient outcomes, and mitigate the incidence of recurring infections. In order to confirm the effectiveness, safety, and clinical utility of nano-emulsion gels in the treatment of UTIs and to facilitate their wider use in clinical practice, more investigation and clinical trials are necessary.

DRUG AND EXCIPIENTS PROFILE

Drug Profile:

Nitrofurantoin

Chemical structure:



Brand Name: Aratoin, Furadantin, Macrobid

IUPAC Name: 1-[(E)-(5-nitrofuran-2-yl) methylideneamino]imidazolidine-2,4-dione.

Appearance: Nitrofurantoin typically appears as a yellow crystalline powder.

Solubility: It is sparingly soluble in water, soluble in organic solvents such as ethanol and methanol.

Melting Point: The melting point of nitrofurantoin ranges from approximately264 to 266°C.

Odour: Nitrofurantoin may have a faint odor.

Molecular Weight: The molecular weight of nitrofurantoin is approximately 238.16 g/mol.

Density: 1.52 g/cm^3.

Stability: It should be stored in a cool, dry place away from light and moisture to maintain stability.

pKa: The pKa value of nitrofurantoin is around 7.1, indicating its acidic nature.

Partition Coefficient (LogP): The LogP value of nitrofurantoin, which indicates its lipophilicity, is approximately 1.4.

Hygroscopicity: Nitrofurantoin may exhibit slight hygroscopic properties, absorbing moisture from the surrounding environment.

Pharmacological Properties:

Belonging to the nitrofuran class of antibiotics, nitrofurantoin predominantly inhibits bacterial DNA synthesis to produce its bactericidal effect. Its antibacterial properties are the result of extensive metabolism in the liver, which produces active metabolites. Escherichia coli, Klebsiella pneumoniae, and Enterococcus species are only a few of them any gram-positive and gram-negative bacteria that are frequently linked to urinary tract infections (UTIs) that the medication has concentration-dependent bactericidal action against.

Clinical Indications:

The main indication for nitrofurantoin is to treat simple urinary tract infections brought on by bacteria that are sensitive. It works very well against acute, uncomplicated pyelonephritis and cystitis, which are lower urinary tract infections. The medication is not advised for the treatment of complex UTIs, such as those brought on by systemic infections, renal impairment, or structural abnormalities of the urinary tract.

Dosage Regimens:

The formulation and the level of infection influence the nitrofurantoin dosage schedule. The usual suggested oral dosage for people for simple lower urinary tract infections is 50 to 100 mg four times a day for five to seven days. Alternatively, a single daily dosage of 100 mg of macro crystal nitrofurantoin or 100 mg of monohydrate/macro crystals (macrobid) nitrofurantoin may be administered for a period of five days. Dosage changes may be required in older patients or those with renal impairment in order to prevent drug buildup and potential toxicity.

Adverse Effects:

Nitrofurantoin is usually well-tolerated, although it can have a number of side effects, including gastrointestinal issues such nausea, vomiting, and diarrhea. Patients may less frequently develop allergic symptoms, such as eosinophilia, pruritus, and skin rash. Chronic nitrofurantoin therapy may cause pulmonary toxicity, which is characterized by acute or chronic interstitial pneumonitis.

This is an uncommon but potentially dangerous side effect. Furthermore, nitrofurantoin may cause peripheral neuropathy, hepatotoxicity, and hematological problems, especially at high doses or after

extended use.

Pregnancy and Lactation Considerations:

Generally speaking, nitrofurantoin is safe to take while pregnant, especially in the first and second trimesters, as there seems to be no increased risk of congenital abnormalities or unfavorable pregnancy outcomes. However, due to the possible risk of hemolytic anemia in babies, especially with extended maternal usage near term, caution is suggested throughout the third trimester. Small levels of nitrofurantoin are excreted in breast milk, and although side effects inner sing in fantsareun common, care should be used when giving the medication to women who are nursing their babies.

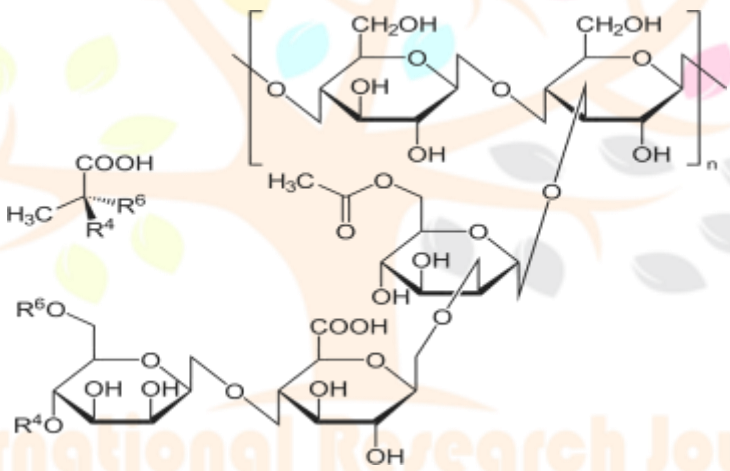
Excipients Profile

1. Xanthan Gum:

Source: Xanthan gum is a natural polysaccharide derived from the fermentation of sugars by the bacterium Xanthomonas campestris.

Properties: Xanthan gum is highly water-soluble and exhibits excellent thickening, stabilizing, and emulsifying properties. It forms viscous solutions and gels when hydrated, making it suitable for various pharmaceutical applications.

Structure



Property	Description
Appearance	White to cream-colored powder
Solubility	Soluble in cold and hot water, as well as in some organic Solvents such as ethanol and glycerol
Viscosity	High viscosity, shear-thinning behavior(viscosity decreases with Increasing shear rate)
Hydration	Rapid hydration in water, forming highly viscous solutions
Texture	Imparts smooth and creamy texture to solutions and suspensions
Stability	Stable over a wide range of pH(2-12) and temperatures (up to 120°C)
Degradation	Resistant to enzymatic degradation.
Synergistic Effects	Exhibits synergistic effects when combined with other effects. Hydrocolloids
Film-Forming	Can form flexible and transparent films when dried
Compatibility	Compatible with a wider range of ingredients, including salts, sugars, and proteins

Function: In pharmaceutical formulations, xanthan gum serves as a versatile excipient, providing viscosity control, stabilization of suspensions and emulsions, and enhancement of drug release and bioavailability.

Applications: Xanthan gum is commonly used in oral suspensions, topical gels, ophthalmic formulations, and controlled-release dosage forms. It is particularly useful in formulations where sustained drug release, enhanced stability, and improved rheological properties are desired.

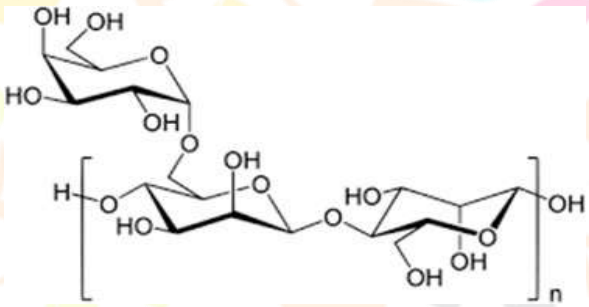
Safety: Xanthan gum is generally recognized as safe (GRAS) by regulatory agencies and is widely used in pharmaceuticals, food, and cosmetic products. It is non-toxic, biocompatible, and well-tolerated, with minimal risk of adverse effects.

2. Acacia Gum (Gum Arabic):

Source: Acacia gum, also known as gum arabic, is a natural gum exudates obtained from the Acacia senegal tree.

Properties: Acacia gum is a complex mixture of polysaccharides and glycoproteins with excellent emulsifying, stabilizing, and film-forming properties. It forms clear, viscous solutions when dispersed in water and exhibits high viscosity and adhesion characteristics.

Structure



Property	Description
Appearance	Amorphous, odourless, colour less to pale yellow powder or granules
Solubility	Highly soluble in water, clear viscous solution; partially soluble in alcohol, soluble in hot glycerine
Viscosity	High viscosity, especially at higher concentrations, varies with Factors like concentration, temperature, and pH
Hygroscopicity	Exhibits hygroscopic properties, absorbing and retaining moisture From the environment
Stability	Stable over a wide pH range (typically pH 3 to pH 11) and Temperature range
Film-Forming	Forms thin, flexible films when dissolved in water, exhibits good adhesion properties
Emulsifying	Acts as an effective emulsifier, stabilizes emulsions and Suspensions
Texture	Enhances mouth feel, contributes to smooth and creamy texture in Food and beverage products
Compatibility	Compatible with a wide range of fooding redients and additives
Reactivity	Inert and non- reactive with most substances, safe for using Various applications

Function: Acacia gum serves as a versatile excipient in pharmaceutical formulations, providing emulsification, stabilization of suspensions, viscosity enhancement, and muco adhesion. It improves the physical stability and organoleptic properties of formulations while promoting controlled drug release and bioavailability.

Applications: Acacia gum is widely used in oral solutions, syrups, suspensions, emulsions, tablets, and lozenges. It is particularly valuable in liquid formulations where viscosity, stability, and patient acceptability are critical factors.

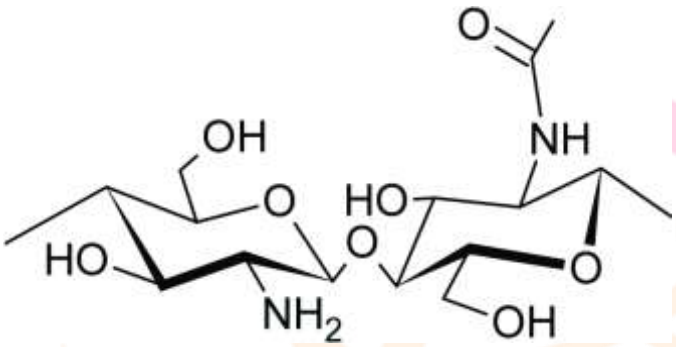
Safety: Acacia gum is considered safe for oral consumption and is approved for use in pharmaceuticals, food, and cosmetic products. It is non-toxic, biodegradable, and well- tolerated, with minimal risk of adverse reactions.

3. Chitosan:

Source: Chitosan is a naturally occurring biopolymer derived from the de-acetylation of chitin, found in the exoskeletons of crustaceans such as shrimp, crab, and lobster.

Properties: Chitosan is a cationic polysaccharide with excellent biocompatibility, biodegradability, and muco adhesive properties. It forms transparent films, hydrogels, and nanoparticles when dissolved in acidic solutions.

Structure



Property	Description
Appearance	White to off-white, odorless, tasteless, and biodegradable Powder or flakes
Solubility	Insoluble in water and most organic solvents; soluble in diluted Acid sand some organic acids
Viscosity	Forms viscous solutions in acidic conditions; viscosity Increases with concentration
Hygroscopicity	Exhibits hygroscopic properties, absorbing moisture from the Environment
Molecular Weight	Variable molecular weight, ranging from low to high, Depending on source and processing
Film-Forming	Capable of forming transparent films when cast from solution
pH Sensitivity	Solubility and properties vary with pH; soluble in acidic conditions, insoluble in alkaline conditions
Biodegradability	Biodegradable under certain conditions, making it Environmentally friendly
Mechanical Strength	Exhibits good mechanical strength and flexibility in film sand Membranes
Compatibility	Compatible with various materials and compounds, facilitating Blending and formulation

Function: In pharmaceutical formulations, chitosan serves as a multifunctional excipient, providing muco adhesion, controlled drug release, wound healing, and antimicrobial properties. It enhances the bioavailability and absorption of poorly soluble drugs and can be used to target specific tissues or organs.

Applications: Chitosan is utilized in various pharmaceutical dosage forms, including films, gels, nanoparticles, micro particles, and scaffolds. It is commonly employed in wound dressings, drug delivery systems, oral formulations, and tissue engineering applications.

Safety: Chitosan is generally regarded as safe for oral and topical use and is biocompatible with minimal toxicity. It is well-tolerated in most individuals, with rare reports of allergic reactions or gastrointestinal

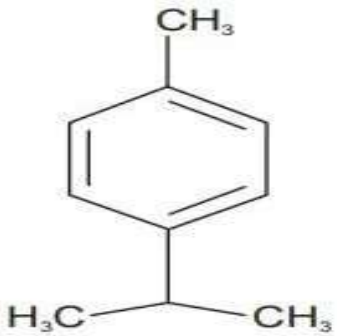
disturbances.

4. Eucalyptus Oil:

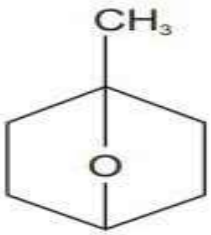
Source: Eucalyptus oil is derived from the leaves of eucalyptus trees, primarily Eucalyptus globules and Eucalyptus radiate, through steam distillation.

Properties: Eucalyptus oil is a volatile essential oil with characteristic aroma and antimicrobial properties. It contains bioactive compounds such as cineole (eucalyptol) and terpenes, which contribute to its therapeutic effects.

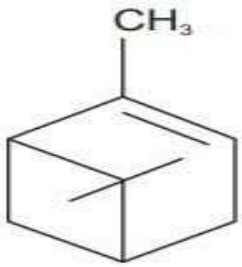
Structure:



p-Cymene



Cineole



α-Pinene

Property	Description
Appearance	Colour less to pale yellow liquid
Odor	Characteristic strong, aromatic odour
Density	0.905-0.925g/cm³ at 20°C
Refractive Index	1.458-1.465 at 20°C
Solubility	Sparingly soluble in water; miscible with ethanol, ether, and Other organic solvents
Boiling Point	Approximately176-177°C
Flash Point	Approximately49°C
Specific Gravity	0.905-0.925 at 20°C
Optical Rotation	Ranges from -10°to+10°, depending on the source and Composition of the oil
pH	Neutral(approximately7)
Stability	Stable under normal storage conditions; may oxidize upon Exposure to air and light

Function: In pharmaceutical formulations, eucalyptus oil serves as a natural antimicrobial agent, decongestant, and expectorant. It exhibits broad-spectrum antimicrobial activity against bacteria, viruses, and fungi, making it useful in the treatment of respiratory infections, wound care, and aromatherapy.

Applications: Eucalyptus oil is commonly used in topical preparations such as ointments, creams, and liniments for its analgesic and anti-inflammatory effects. It is also incorporated into oral products like lozenges, mouthwashes, and throat sprays for its antiseptic and refreshing properties.

Safety: Eucalyptus oil is generally safe for topical and aromatic use when properly diluted. However, it can be toxic if ingested in large quantities and may cause adverse reactions.

Preparation of Nano-emulsion (NE)

The previously mentioned procedure was followed to prepare the nano-emulsion[50] with slight modifications. For the creation of nano-emulsions, high-speed stirrers and high- speed homogenizers (Remi) were employed. To create the oil phase (A) of the nano-emulsion, 10 g of eucalyptus oil and 25 g of NGB were combined. The oil phase received the medication addition. 39.9 g of distilled water and 25 g

of tween-80 (Polysorbate-80) were combined to create the aqueous phase (B). Before the nano-emulsion was prepared, both phases (A+B) were maintained on a water bath (Labco, Model 345, India) for thirty minutes at a temperature of 45 ºC ± 5Following the heating of both phases, the oil phase was gradually added to the aqueous while being stirred vigorously (3500rpm) for seven minutes. The mixture was progressively cooled, and the stirrer's speed was lowered to 1400 rpm for duration of 12 minutes. In order to achieve uniform mixing, the stirrer's speed was increased once more to 3500rpm for 12 minutes, or until a uniform emulsion was achieved. The emulsion was given at least one hour to cool. For 12 minutes, this emulsion was run through a high speed /high shear homogenizer at 14000 rpm. Several formulations including varying amounts of components were created and stored for initial stabilities with the aim of optimisation.

RESULT:

The formulations included eucalyptus oil nano-emulsion, chitosan based nano-emulsion gel, and blank formulations. Periodically, the phase separation, consistency, liquefaction, colour change, and cracking of these compositions were assessed physically. The formulations were all thermodynamically stable based on the characteristics mentioned. Droplet size, polydispersity (PDI) and surface charge. When it comes to formulations used for topical or transdermal medication administration, droplet size is crucial. The droplet size and size distribution have an impact on a number of promising factors, including medication release, drug penetration, and bio distribution. The ATR-FTIR spectrum was used to distinguish between the functional groups present in pure chitosan and chitosan-loaded eucalyptus oil nano-emulsion. The % drug content in any pharmaceutical composition verifies the uniform distribution of medicines. The drug content results showed that the percentage of drug content was within the official limit, which is 100±10% of the US Pharmacopoeia (USP). Drug delivery through topical or transdermal application is significantly impacted by viscosity; viscosity affects stability, Spreadibility, drug release, and application ease. Other factors that can affect viscosity of formulations include the type of gelling agent used, the emulsifiers (surfactants and co-surfactants), the oils and co-solvents used in the formulations, and others. Spreadibility is the degree to which a pharmacological formulation administered topically disperses across skin. The essential component of topical formulations that determines the therapeutic efficacy is Spreadibility. Similar to this, topical formulations' viscosity decreased at high temperatures, leading to their considerable Spreadibility. The release of a medication from its pharmaceutical dose form determines its therapeutic efficacy. The antibacterial activity of the formulation against various strains of bacteria, including *Pseudomonasaeruginosa*, *Escherichiacoli*, *Proteusmirabilis*, and *Klebsiella pneumonia*, was evaluated in terms of the zone of inhibition (ZOI). The results indicated that the formulation exhibited significant antibacterial activity against all tested uro pathogenic strains, with increasing concentrations leading to larger ZOI values.

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