TO DEVELOP NANOPARTICLE FORMULATIONS OF THE PIROXICAM MEDICATION UTILISING VARIOUS POLYMERS

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ABSTRACT:

Nanoparticles are formulated to target the drug to the specific organ site and to control the rate of delivery of drug. By encapsulating a drug into nanostructures, the being of the drug in the systemic circulation can be prolonged and decrease the toxicity. The main aim of this study is to achieve prolonged release of Piroxicam such that the dosing frequency of the drug can be reduced by which we may decrease the side effects and improve the patient compliance. Investigation of the preparation, characterization and in-vitro delivery of the nanoparticles was carried out. Eight different formulations with different concentration of drug-polymer and surfactant were prepared and evaluation were done like in vitro drug release, kinetic studies and stability studies. Nanoparticles were then characterized for entrapment efficiency, percent yield, particle size analysis, morphological characteristics, and in vitro drug release the prepared particles showed good drug-loading capacity. Formulation (F-4) showed the highest encapsulation efficiency. It was concluded that F4 formulation is the optimized formulation.

***Keywords**: Piroxicam, polymers, solvent evaporation technique, Franz diffusion cell, encapsulation efficiency stability studies.*

INTRODUCTION

Drugs or other active molecules of nano-liposomal type can be transported in nanoparticles, which are transport compartments for nanoparticles (10-1000nm). The biodegradability, nontoxicity, and long-term storage of nanoparticles make them excellent drug delivery vehicles. Nanoparticles are effective in delivering medications to the liver and cells that are active phagocytically because they are taken up by the reticuloendothelial system following intravenous delivery. Consequently, nanoparticles can be utilised as isometric carriers. ' In addition, it is feasible to improve nanoparticle transport to the spleen in comparison to the liver by altering the surface features of nanoparticles by coating them with chemicals such as surfactants. The advantages of nanoparticle compositions are numerous. Pure drug nanoparticles show promising outcomes in delivering medications to diverse organs and via different pathways. Biodegradable and biocompatible polymeric carriers have greatly affected the controlled and targeted medication delivery idea. The exceptional physical and chemical capabilities that nano materials, such as nanoparticles, nano tubes, and thin films, have as a result of the nano size effect, make their creation critical to the advancement of nanotechnology. A lot of people are excited about the possibilities of nano medicinals in the diagnostic and therapeutic domains. Specifically, nanoparticle drug delivery presents novel

therapeutic opportunities for active agents (drugs or genes) previously unsuitable to traditional oral (or) injectable therapeutic formulations, allowing active agents to be delivered efficaciously while minimizing side effects and leading to better patient compliance. In principle, nanotechnology might minimize the cost of drug discovery, design, and development. Miniaturization, automation, speed, huge parallelism, and reproducibility of tests should improve the drug discovery process itself. As a physical approach to improving the pharmacokinetic and pharmacodynamic features of numerous types of pharmacological molecules, nanoparticles have been employed for the past few decades as a method of drug delivery. Novel medication delivery systems have received a lot of attention during the previous two decades. A new approach for producing water-soluble nanoparticles has been disclosed. Drugs that are less than 100nm in diameter are better able to pass biological cell membranes and reach their target spot because of their smaller size. 7 Antihypertensive medication therapy is plagued by several difficulties, and a novel drug delivery mechanism provides formulation scientists with an opportunity to solve these difficulties. ACE inhibitors, angiotensin antagonists, calcium channel blockers, diuretics, central sympathomimetics alpha-adrenergic blockers, vasodilator, beta-adrenergic blockers are some of the currently available antihypertensive medications.

Preparation of nanoparticles

Nanoparticles can be made using a variety of methods, depending on the medication to be loaded and the polymer's physicochemical qualities. Nanoparticles can be made in a variety of ways, including:

Emulsion-Solvent Evaporation Method

The majority of nanoparticles are made this way. This approach consists of only two phases. The first step is to emulsify the polymer solution in an aqueous phase. While in the second stage, the polymer solution evaporates and the precipitation of nanospheres is induced. For preservation, nanoparticles are lyophilized after being collected using ultracentrifugation and then washed with distilled water to eliminate any free drug or residue. Solvent evaporation technique and high-pressure emulsification are other names for this procedure. Homogenization under high pressure and general stirring is employed to eliminate organic solvents.

The size may be modified by altering the stirring rate, a viscosity of organic and aqueous phases, temperature, type and amount of dispersion agent. In the case of lipid-soluble medicines, however, this method can be used and scale-up concerns impose limitations. Polymers utilised in this process include PLA, Poly (-hydroxybutyrate), Poly (caprolactone), Poly (caprolactone), Poly (caprolactone), Poly (caprolactone), PLGA, and cellulose acetate phthalate (EC).

Double Emulsion and Evaporation Method

The primary downside of this approach is poor drug entrapment for hydrophilic drugs. Hydrophilic drugs can be packaged using the double-emulsion approach, which involves the addition of aqueous

drug solutions to an organic polymer solution that is vigorously stirred. This w/o emulsion is incorporated into another aqueous phase utilizing continuous stirring. Then the solvent is evaporated, and nanoparticles may be separated by centrifugation at high speed. The produced nanoparticles must be cleaned before lyophilization. The amount of hydrophilic drug, polymer, aqueous phase volume, and stabiliser concentration are all factors in this procedure. Variables such as these can impact the characterisation of nanoparticles as well.

Literature REview

Gaber, D. A.,(2023) Piroxicam nanosponge formulations were characterized for its particle size, zeta potential, physical compatibility and in vitro release. Stability studies at three temperatures (4 °C, 25 °C and 40 °C) were done for optimal formula. Finally, the in vivo analgesic activity and pharmacokinetic parameters of the optimal formula were conducted. The optimized PXM-NS formula (PXM-NS10) showed particle size (362 ± 14.06 nm), polydispersity index (0.0518), zeta potential (17 ± 1.05 mV), and %EE (79.13 ± 4.33). The dissolution study showed a significant increase in the amount of PXM dissolved compared with the unformulated drug. Stability studies confirmed that nanosponge showed accepted stability for 90 days at 4 °C and 25 °C. In vivo analgesic studies verified that there was a significant enhancement in the analgesic response to PXM in mice, and 1.42 fold enhancement in the relative bioavailability of PXM-NS10 as compared to commercial tablets. Nanosponge prepared under optimal conditions is an encouraging formula for increasing the solubility and therefore the bioavailability of Piroxicam.

Rahmani Del Bakhshayesh (2020) Piroxicam (PX), a main member of non-steroidal anti-inflammatory drugs (NSAIDs), is mainly used orally, which causes side effects of the gastrointestinal tract. It also has systemic effects when administered intramuscularly. Intra-articular (IA) delivery and encapsulation of PX in biodegradable poly-ε-caprolactone (PCL) nanoparticles (NPs) offer potential advantages over conventional oral delivery. The purpose of this study is the development of a new type of anti-inflammatory bio-agents containing collagen and PX-loaded NPs, as an example for an oral formulation replacement, for the prolonged release of PX. In this study, the PX was encapsulated in PCL NPs (size 102.7 ± 19.37 nm, encapsulation efficiency 92.83 ± 0.4410) by oil-in-water (o/w) emulsion solvent evaporation method. Nanoparticles were then characterized for entrapment efficiency, percent yield, particle size analysis, morphological characteristics, and *in vitro* drug release profiles. Eventually, the NPs synthesized with collagen were conjugated so that the NPs were trapped in the collagen sponges using a cross-linker. Finally, biocompatibility tests showed that the anti-inflammatory agents made in this study had no toxic effect on the cells. Based on the results, it appears that PX-loaded PCL NPs along with collagen (PPCLnp-Coll) can be promising for IA administration based on particulate drug delivery for the treatment of arthritis.

Soliman Mohammadi-Samani (2018)
Piroxicam loaded SLNs were formulated by solvent emulsification/evaporation method. Particle size assessment, entrapment efficiency assessment, *in vitro* release study and skin permeation of the piroxicam were carried out to characterize the SLNs. These SLNs were then formulated in gel as a topical delivery system to assess percutaneous permeation of piroxicam. The SLNs were prepared in different size ranges from 100 to 300 nm and drug release behavior from two different nano-sized SLN suspensions was evaluated. Piroxicam nanolipidic gel exhibited increased skin permeation of the drug over commercial piroxicam gel formulation and also mean particle size of formulated SLNs had a significant effect on permeation rates.

RESULTS AND DISCUSSION

We created eight different formulations with varying polymer concentrations and ran physicochemical tests, in vitro release tests, and stability tests on them.

Preformulation studies

Table - Organoleptic properties of Piroxicam

Properties	Results
Description	powder
Taste	Tasteless
Odour	Odourless
Colour	White

Drug profile

DRUG PROFILE Piroxicam

Name: piroxicam

Category: nonsteroidal anti-inflammatory drug (NSAID)

Molecular Structure:

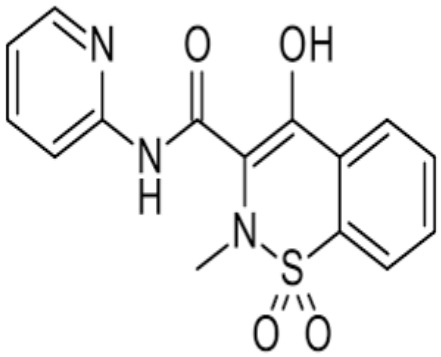

Fig : Molecular structure of piroxicam

Synonyms: Feldene, Piroxicamum, Pyroxycam

IUPAC Name:4-hydroxy-2-methyl-1,1-dioxo-N-(pyridin-2-yl)-2H-1λ⁶,2-benzothiazine-3-carboxamide

Molecular Formula: C15H13N3O4S

Molecular Weight: 331.3 g/mol

Description: Rheumatoid arthritis and osteoarthritis have long been successfully treated with this NSAID, which is also commonly used to alleviate muscle pain, menstrual irregularities, and postoperative discomfort. It is cyclooxygenase inhibitory. It can be taken once a day because of its lengthy half-life.

State: Solid

Melting point: 198-200 °C Solubility: Poisoned water, alcohol and alkaline aqueous solutions can be used to dissolve Piroxicam. Methylene chloride can be used to dissolve Piroxicam in the presence of an acidic solution.

Standard graph of Piroxicam in pH 7.4 buffer

Over a concentration range of 10 to 50 g/ml, the solution followed Beer-law Lambert's with a regression coefficient of 0.998. The in vitro samples of Piroxicam were estimated using this standard curve.

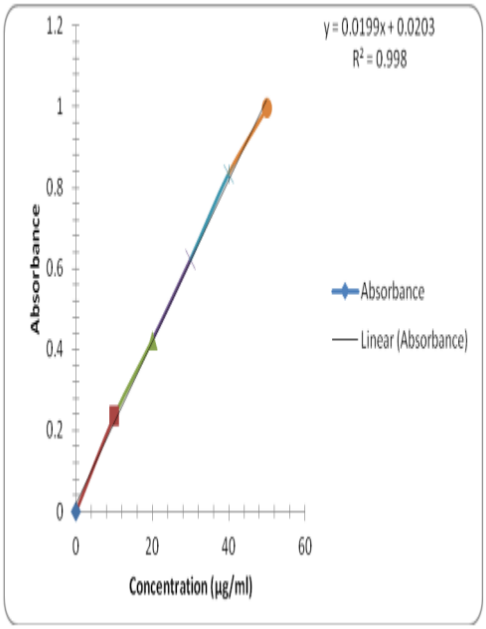

Fig-Standard graph of Piroxicam in pH 7.4 buffer

Drug - excipient compatibility studies (FT-IR)The FTIR peak matching approach was used to determine the drug's compatibility with the chosen lipid and other excipients. The absence of peaks in the drug-lipid combination proved the lack of chemical interaction between the medication, lipid, and other molecules.

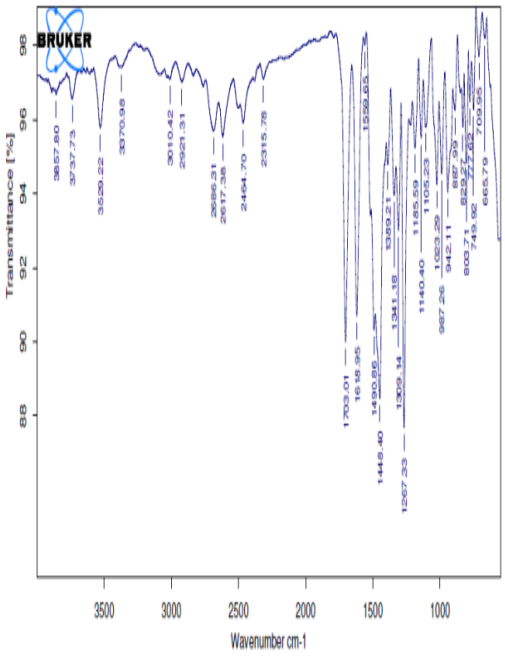

Fig - FT-IR Sample for Piroxicam

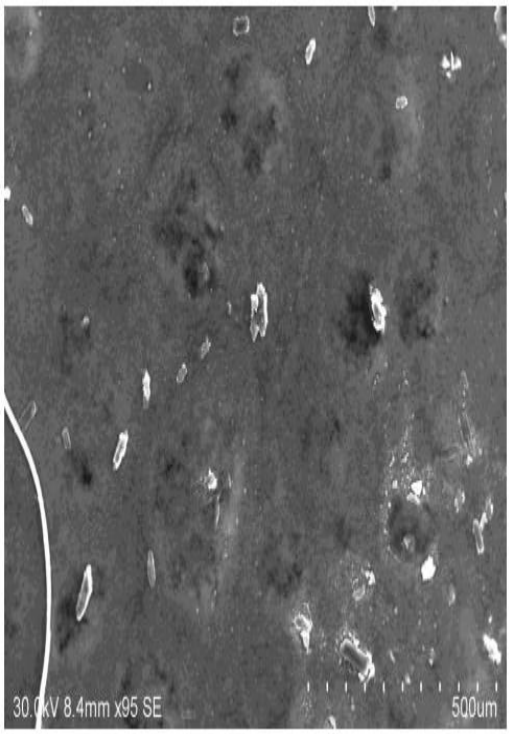

Fig - SEM analysis of Optimized Nanoparticles

Assayed drug content and encapsulation efficiency of nanoparticles were found to be favourable in the study results. There

was a decent yield and it was appropriate and repeatable from the process utilised for formulation. The encapsulation efficiency of the formulation (F-4) was the greatest. The percentage of encapsulation efficiency rose as the concentration of chitosan increased. Following the approach described, dialysis membrane permeation investigations were conducted. After an initial burst effect, there was a gradual release of drugs from the polymer in the in vitro test results of all the formulations. Drug molecules that disperse near the nanoparticle surface and quickly diffuse during the initial incubation time are thought to be responsible for the burst release of the drug. Piroxicam was released more quickly from nanoparticles with a larger concentration of the medication.

CONCLUSION

Piroxicam Nanoparticles for controlled release were developed in this study using a new formulation. It was discovered how the Nanoparticles are made, characterised, and released in vitro. Different drug-polymer and surfactant ratios were examined and adjusted for different formulations. A high level of drug encapsulation efficiency has been attained in this investigation. Piroxicam nanoparticles were synthesised using a solvent evaporation approach, then sonication was utilised to lower the particle size.

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