Solubility enhancement of meloxicam by phospholipid complexation

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INTRODUCTION

Meloxicam (MLX) and other non-steroidal anti-inflammatory medicines (NSAIDs) selectively inhibit the COX-2 enzyme's inducible isofrom. The catalyst is the prostaglandin synthesis enzyme COX-2, which has been well investigated for its possible connection to the onset of cancer. It influences apoptosis, angiogenesis, and is connected to the creation of carcinogens. 1, 2 MLX which is a member of BCS class II, has demonstrated anticancer efficacy. 3 MLX is a medication that is commonly used to treat inflammation and is taken orally in the form of a regular tablet. The limited aqueous solubility of MLX, however, placed some restrictions on its clinical usage in cancer therapy. Even yet, after the MLX’s solubility was improved, the increased permeability might be advantageous. The amount of literature on the use of MLX in cancer treatment was quite restricted. Therefore, it is necessary to investigate MLX’s potential as a cancer treatment. Additionally, designing the job is necessary to increase MLX’s solubility.

The phospholipids complexation method is the most effective way for increasing solubility 4, and multiple authors have used it to successfully increase the solubility, permeability, and oral bioavailability of plant bioactives and extracts. Phospholipon® 90H, the system’s major component, functions in a manner akin to that of plasma membrane phospholipids. 5, 6 The phosphate (+) charged Phospholipon® 90H can successfully interact with any lipophilic drug's polar components to create an amphiphilic molecule. 7

In the current study, an effort was made to increase the solubility of meloxicam. Based on the phospholipid complex system’s beneficial solubility enhancing effects, it is classified as BCS class II. Therefore, the development and evaluation of the meloxicam-phospholipid complex for solubility augmentation was the study’s main objective.

MATERIAL AND METHODS

Ramdev Chemicals Pvt. Ltd., Thane, (Maharashtra), India, gave us meloxicam (MLX) as a gift sample. We purchased Phospholipon® 90H from Lipoid GmbH In Ludwigshafen, Germany. Analytical grade chemicals and other reagents were used.

Preparation of MLX-phospholipid Complex

Meloxicam-phospholipid complex was synthesized by modifying a method for solvent evaporation that had previously been described. 7, 8 A solution of 1.5 mL of DMSO and 2 mL of chloroform was used to dissolve about 100 mg of MLX. About 100–300 mg of Phospholipon® 90H were added to this solution, and 1,4-dioxane was then added to further dissolve it. The entire mixture was then refluxed for 4–6 hours on a water bath at 60 to 70 °C. After being heated in a water bath, the reaction mixture was let to condense. Approximately 3–4 mL of n-hexane were added to this saturated mixture. The next day, the supernatant was decanted and dried at room temperature. Stored and used for additional examination.

Abstract

The best solubility enhancement approach is phospholipids complexation. It has been effectively employed by a number of writers to enhance the permeability, oral bioavailability, and solubility of several medicinal substances. The meloxicam is a member of BCS class II, and because of its poor solubility and high permeability, its clinical application may have been constrained. Therefore, it is necessary to use a method that modifies the biopharmaceutical features. In this work, meloxicam, an NSAID with demonstrated anticancer action, was combined with phospholipid to increase its solubility. Utilizing solvent evaporation, the meloxicam phospholipid complex was produced. Particle size, zeta potential, SEM analysis, in vitro drug release, and solubility were assessed for the produced complex. The results obtained in this study showed the smaller particle size in nanometer range and physical stability with desired zeta potential. Meloxicam’s prolonged release from the phospholipid complex is demonstrated by the in vitro drug release investigation. The apparent solubility analysis of meloxicam phospholipid complex. Pure meloxicam showed that the drug’s solubility was several times higher than that of the pure form. Hence in conclusion we can say that the phospholipid complexation could be the ideal method for solubility enhancement of drug like meloxicam.

Keyword: Meloxicam, phospholipid complex, solubility, drug release
Physicochemical analysis

Particle size and zeta potential

The formulated MLX phospholipid complex’s particle size and size distribution were assessed using the DLS-based technique. In brief, 5.0 milligram dried MLX phospholipid complex was transferred and distributed using cuvettes-containing de-ionized water. At 25 °C, measurements were taken within the Malvern Zetasizer instrument chamber. Using a Malvern Zetasizer nano sizing device, the zeta potential of the MLX phospholipid complex was calculated between the ranges of -200 and +200 mV.10,11

FTIR spectroscopy

In a nutshell, pre-treatment was applied to the MLX and MLX phospholipid complex sample before FTIR analysis. These materials were mixed evenly with potassium bromide (KBr) of FTIR grade in a 1:100 ratio. After that, these were analysed using 45 scans at a resolution of 4 cm⁻¹, covering a range of 4,500 to 400 cm⁻¹.12

Scanning electron microscopy

Examining the morphological structural properties has been done using scanning electron microscopy (SEM). On a specimen tab, a little amount of the MLX phospholipid complex was put before being transferred to a slide. The sample was prepared for SEM microscopic examination after palladium coater was applied. Then, SEM images were taken utilising a Carl Zeiss lens and a JEOL scanning electron microscope.

In vitro drug release study

The in vitro drug release study was conducted using the approach outlined in previous publications.14 In a nutshell, the Franz diffusion cell (donor compartment) was filled with an aqueous suspension of the MLX phospholipid complex. The pH 7.4 phosphate buffer saline was poured into the receptor compartment. The donor and receptor chambers of the diffusion cell were placed apart by the dialysis membrane. An aqueous solution containing 20 mg of MLX phospholipid complex powder, which is equivalent to 10 mg of medicine, was injected into the donor compartment. Periodically, samples from the side arm were taken, and an equivalent volume of pH 7.4 PBS was added to the medium to restore it. The collected samples were measured with a UV spectrophotometer at 362 nm.

Solubility analysis of phospholipid complex

The concentration of the material in the solvent at supersaturation equilibrium is indicated by the apparent solubility. Using a modified approach that was previously published, we investigated the apparent solubility of MLX and the MLX phospholipid complex in this study. To make a dispersion, approximately 5 mg of MLX and MLX phospholipid complex were combined with 5 mL of clean water and n-hexane. This was centrifuged for 30 minutes at 4000 RPM after being constantly mixed for 24 hours at 25°C. Centrifugation was used to extract the supernatant. The collected supernatant was then filtered using a membrane filter (0.45) to eliminate any insoluble particle debris. After the filtrate was filtered and diluted with DMSO, the concentration of MLX at 362 nm was measured using a UV-spectrophotometric technique.

RESULT AND DISCUSSION

Physicochemical characterization

Previous studies showed that the micro-sized particles of the original drug or material were substantially less bioavailable than the particles with a size between 200 and 400 nm.15,16 Zetasizer measurements showed that the particle size of the MLX phospholipid complex was approximately 122 nm. However, it was found that the zeta potential of the MLX phospholipid complex was 35.8 mV, which is lower than 30 mV. It proved the remarkable physical stability of the MLX phospholipid complex.17,18 The zeta potential likewise rises as the surface charge does.19

FTIR analysis

The NH₂ scissoring vibrations band is at or near 1619 cm⁻¹, the secondary amine stretching band is at or near 1550.04 and 1530.36 cm⁻¹, the C-N stretching band is at or near 1550.04 and 1530.36 cm⁻¹, and the S-O stretching band is at or near 1346.73, 1265.88, and 1183 cm⁻¹ as shown in figure 1A. According to figure 1B, FTIR spectrum of MLX phospholipid complex shows peaks with similar stretching frequencies and negligible shifts from 3285.45, 1616.88, and 1061.17 cm⁻¹ demonstrated the low intermolecular interaction between MLX and phospholipid. The overall FTIR result was interpreted as indicating that the ingredients used to prepare the MLX phospholipid complex did not interact and found to be compatible.
Scanning electron microscopy

SEM was used to study the surface morphology of the MLX phospholipid complex, and structural features were found by looking at SEM pictures, as figure 2 illustrates. The rough surface of the MLX phospholipid complex is shown in this picture. A solvent or other fluid could reach the porous surface of the complex and begin the solubilization process.

In vitro drug release study

A buffer pH 7.4 was used for the drug release study of MLX from the MLX phospholipid complex and MLX solution. The findings of this investigation showed that the initial burst release of MLX was determined to be around 26% in the first two hours, and the 94% release of MLX was recorded after 72 h. However, as seen in the figure 3, MLX solution releases around 94% of the drug in just 6 hours. Therefore, based on these findings, we can say that drugs are released under controlled conditions over a longer period of time. 20, 21
Apparent solubility analysis

A study on the solubility of MLX and the MLX phospholipid complex in water and other organic solvents revealed improved solubility. In comparison to the MLX, the MLX phospholipid complex exhibits improved solubility and dissolving behavior. After creating the MLX phospholipid complex, the solubility of MLX was shown to have risen many folds.

CONCLUSION

The MLX phospholipid complex was made using the solvent evaporation method. The production of phospholipid complexes may increase a medicine’s solubility if it is just marginally soluble in water. Compared to pure MLX, the produced MLX phospholipid complex dissolves more readily in water. The improved MLX phospholipid complex showed reduced particle size and prolonged drug release over a 72-hour period. The overall findings of this investigation demonstrated the superb potential of phospholipid complex for improving solubility.

CONFLICT OF INTEREST

Authors declared no conflict of interest.

REFERENCES


