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Separation Of Ibuprofen Enantiomers With Modification Of A Pre-Coated Silica Gel To A Chiral Tlc Plate

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***Abstract*— Ibuprofen is a non-steroidal anti-inflammatory drug used against pain, possessed analgesic, antipyretic and anti-inflammatory properties. A simple cheap eco-friendly TLC method was developed in order to separate racemic drug substance and directly to determine the isomers without using expensive instruments and additional substances. The separation was achieved using L-arginine where R_f values were 0.82 and 0.79 for (*S*)-(+) and (*R*)-(-) ibuprofen, respectively. A routine method for the analysis of ibuprofen could be used in further research.**

***Keywords*— ibuprofen, TLC, racemic mixture, chirality**

I. INTRODUCION

Inflammation plays an important role of the immune system's response to heal and repair damaged cells and tissue. The most common conditions where the body suffers are redness, heat, swelling, and pain [1]. Moreover, the inflammation protects the human body from bacteria and viruses. The therapeutic effects are classified as anti-inflammatory, analgesic and antipyretic [2].

Ibuprofen belongs to a class of pharmaceuticals referred to as non-steroidal anti-inflammatory drugs. Primarily, the drug is used in the treatment of fever, painful menstruation, dental pain, headaches, rheumatic diseases of the joints and the soft tissues [3-5].

Ibuprofen contains a chiral carbon and from the formula, 2^n, where *n* is the number of chiral atoms, therefore two enantiomer forms are present, (*S*)-(+)-enantiomer and (*R*)-(-)-enantiomer, while (±)-ibuprofen refers to the racemic mixture which is available for the consumers. Between two enatiomers, (*S*)-(+)-enantiomer is the isomer with the possession of biological activity form both models *in vitro* and *in vivo* and the other form is practically inactive. Although, the (*R*)-(-)-enantiomer is not harmful, it was shown that the pure (*S*)-(+)-enantiomer is more effective against problematic health conditions. The different biological effects regarding to both isomers of ibuprofen resulted in improving of the selectivity and potency of ibuprofen formulations leading to be a single-enantiomer product [6]. The most common methods for separation of ibuprofen enantiomers are HPLC [7] using UV detector [8] and capillary electrophoresis [9]. The approaches in previous studies are either with derivatization procedure where the throughput of the separation is time consuming or problematic adjustment of pH in improving the separation [9].

In order to overcome problems such as consumption of solvent as mobile phase or an expensive instrumentation, an easy to handle and a cheap TLC method with a modified pre-coated silica gel to a chiral TLC plate with pretreatment approach of the pre-coated silica gel TLC plate with D-(-)-tartaric acid and using L-arginine for the determination of ibuprofen enantiomers was introduced.

II. Materials and Methods

Merck (Germany) supplied analytical grade methanol, tartaric acid, sodium potassium tartrate tetrahydrate, D-(-)-tartaric acid, L-arginine, ethyl acetate, and glacial acetic acid. Water was double distilled. Commercially available ibuprofen in tablet form was compared with (±)-ibuprofen from Merck (Germany) used as a standard in the analysis. The TLC was carried out using Merck pre-coated plates (60 F_{254}, 250 µm) and the plates development were visualized directly using an Analytikjena (Germany) ultraviolet lamp at 254 nm. A mixture of mobile phases such as methanol and water (1:1 *v*/*v*); ethanol; ethyl acetate and glacial acetic acid (9:1 *v*/*v*) were used in the analysis. The modification of pre-coated TLC plate to chiral one was achieved with conventional dipping impregnation method of the commercially available TLC plates into the solution of a chiral separator either L-arginine or D-(-)-tartaric acid. The plates were left to be dried at ambient temperature (25 ºC) in the air [10]. The TLC plates were once again dried and the developed lanes were evaluated under ultraviolet lamp at 254 nm.

III. Results and Discussion

The analytical purity was indicated with TLC where the R_f values were depended on the use of the mobile phase as well as the preparation of the TLC plate. The obtained R_f values were compared to the standards and was recorded on 0.7 without any

pretreatment [5] of the plate using the mobile phase consisted of ethyl acetate and glacial acetic acid (9:1 *v*/*v*). The results showed that the values of R_f when the plates were firstly impregnated in tartaric acid were 0.84, 0.89, and 0.83 using methanol and water (1:1 *v*/*v*), methanol, and ethanol, respectively. A value for R_f of 0.83 was recorded when the plate was firstly impregnated in the methanolic solution of sodium potassium tartrate tetrahydrate, while a value of 0.85 was achieved when a commercially available pre-coated TLC plate was developed with methanol as a mobile phase. The stereometric separation was achieved using L-arginine where R_f values were 0.82 and 0.79. In the comparison to the literature [10] study has shown that the separation of the enantiomers could be achieved in the densitometric assessment where the R_f values were 0.82 and 0.79 for (*S*)-(+) and (*R*)-(-), respectively.

IV. Conclusion

The enantiomer separation of ibuprofen was achieved using modified pre-coated TLC silica gel plates to chiral one prepared in laboratory. One spot on the silica gel TLC was recorded without modification of the TLC plate and two spots using the modified TLC plate in pharmaceutical analysis of ibuprofen as an analgesic drug. A simple, economic, and eco-friendly method in terms of not using great amount of substances and solvents was developed for the determination of ibuprofen. The proposed method enables directly determination of the drug sample without reagents for derivatization. In addition, this method does not require expensive equipment and toxic reagents.

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