Chapter

Biological Evaluation and Molecular Docking Studies of Benzalkonium Ibuprofenate

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Abstract

The third-generation ionic liquids (ILs), which are being used to produce double active pharmaceutical ingredients (d-APIs) with tunable biological activity along with novel performance, enhancement, and delivery options, have been revolutionizing the area of drug discovery since the past few decades. Herein we report the in vitro antibacterial and anti-inflammatory activity of benzalkonium ibuprofenate (BaIb) that are being used as in-house d-API, with a particular focus on its interaction with respective protein target through molecular docking study. The evaluation of the biological activity of BaIb with the antibacterial and anti-inflammatory target at the molecular level revealed that the synthesized BaIb could be designed as a potential double active drug since it retains the antibacterial and anti-inflammatory activity of its parent drugs, benzalkonium chloride (BaCl) and sodium ibuprofenate (NaIb), respectively.

Keywords: benzalkonium ibuprofenate, double active pharmaceutical ingredient, molecular docking studies, anti-inflammatory, antibacterial activities

1. Introduction

In the pharmaceutical field, ionic liquids (ILs) by salification of drugs were widely applied to improve the performance of drugs on its oral administration, especially, their solubility, bioavailability, and stability. The research on the antimicrobial activity of ILs is a growing field because of its unprecedented flexibility for chemical diversity in a severely drained arsenal of antimicrobial. The third-generation ionic liquids give us the freedom to tune the biological properties in addition to its physical and chemical properties. The proper selection of ions with synergetic effects may result in the formation of double active pharmaceutical ingredient (d-API). Thus the d-APIs are composed of asymmetric organic ions, which prevent the formation of the stable crystal lattice and are liquid at unusually low temperatures. Such d-APIs can be used for the ailment situations where the two activities are required. This strategy will reduce the excess in taking of unwanted chemicals and will enhance the solubility and bioavailability [1, 2].

Benzalkonium ibuprofenate (BaIb) is a double active pharmaceutical ingredient designed by combining benzalkonium cations with ibuprofen. Benzalkonium chloride

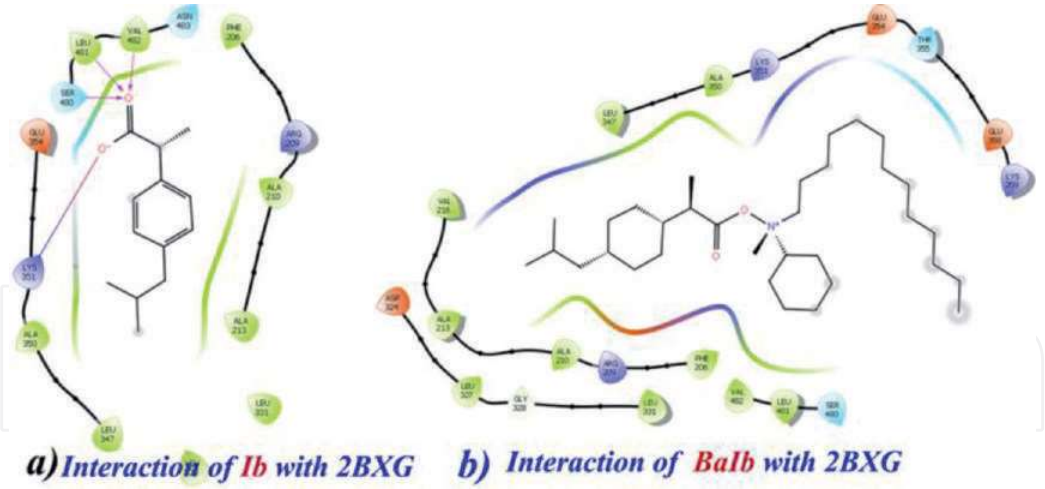

Figure 5.
Schematic representations of ligand-protein interaction and binding interaction using stick mode. (a) Ibuprofen with 2BXG and (b) BaIb with 2BXG using Schrodinger software.

HSA protein as similar to the native ligand ibuprofen by forming a hydrogen bond with active site amino acid.

4. Conclusions

In this work, the biological evaluations of a synthesized double active pharmaceutical ingredient BaIb were done to confirm the retainity of the biological activities of its parent drugs and to elucidate information regarding its potential activities against their respective ailments. Further molecular docking studies were done to get a better understanding about the mode of interaction of the parent as well as daughter drugs with the targeted proteins and trace out the binding pore and cites in the targeted proteins.

The in vitro studies revealed that the synthesized BaIb could be designed as a potential double active drug since it retained the antibacterial activity of its parent BaCl with considerable inhibitory action against *E. coli* and *P. aeruginosa* compared to the parent drug. The binding energy and docking score of BaCl and BaIb again confirm that the prepared d-API BaIb docks well into the LpxC proteins of *E. coli* and *P. aeruginosa* with high docking and Glide score compared to the parent drug BaCl.

Similarly, the results from both in vitro and in silico method emphasize that the prepared d-API retained the anti-inflammatory action of its parent NaIb and bound well to the deep pocket of the active site in the human serum albumin. Thus, in total, one can conclude that the prepared BaIb can be used as a potential double active drug with antibacterial and anti-inflammatory actions.

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