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Commentary on: *In Silico* Design and Pharmacological Evaluation of Conjugates of Atenolol with Modified Saccharides for Cardiovascular Targeting

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Abstract:

The sugar-macromolecule conjugates-based drug delivery systems are discovered to be more successful targeted drug delivery systems needed for targeting the particularity of cardiovascular medications. The planned medication transporter biomolecules complex surface will comprise of saccharide layer to minimize nonspecific interactions, and to mediate selective receptor focusing on.

Use of glycoconjugates in particular drug delivery to limit drug loss by degradation, prevent harmful side effects, and increase bioavailability is affirmed and aftereffects of cell line studies may yield evidence for specific heart delivery. This methodology of upgrading delivery and pharmacological impact of medication by conjugating it with the biodegradable and biocompatible polymeric system is relied upon to improve the selectivity of medication delivery for the treatment of cardiovascular diseases.

The main purpose of the article was to conjugate the cardiovascular drug with the modified Saccharide for cardiovascular targeting. Drug release analysis and cellular uptake study were carried out using H9c2 cell lines. Brine shrimp lethality bioassay was carried out to investigate the cytotoxicity of synthesized complex and conjugates. In silico analysis was performed to assess the possible binding of the developed conjugates with the GLUT-4, Homology model of the GLUT-4 was developed using the SWISS-MODEL server.

Keywords: *Biopolymer; Galactose; Pectin; Chitosan; Chemical modification; Atenolol*

Introduction

Cardiovascular infections are one of the leading causes of mortality and morbidity in developed as well as developing countries and have become a critical medical issue for all countries because of the unstoppable trend of aging and obesity in the population [1]. Thus, although there are systemic medications for some cardiovascular diseases, the available approaches of drug therapy face a critical problem of a variety of side effects due to the presence of the target for a drug at various organs and systems. Few of them also create other pathological complications. Hence, it is much needed to address the issue by reducing side effects and improving drug delivery specific to the ideal site of activity. Hence, exploration of approaches for targeted drug delivery can be utilized to increase the specificity of biological action without the side effects. This can also cause a reduction in doses further improving the safety of the drug therapy [2-6].

Monosaccharide and polysaccharide polymers obtained from the natural origin are non-toxic, biocompatible, and biodegradable. Additionally, polysaccharides are more thermally stable than other biopolymers, like lipids and proteins [7]. According to Manandhar S, et al. (2021) [8], incorporation of the drug into a chemically modified polymeric matrix might protect the biologically active compound from improving absorption, degradation; enhance the therapeutic efficacy, control drug release, and so lead to the decrease in the frequency of administration. The monosaccharide, Galactose is an aldohexose that naturally occurs in D-form in lactose and also C4 epimer of glucose [2, 9]. As per the literature [10, 11], the polysaccharide, Pectin's are made of several sugar derivatives, the most significant of which are the rhamnogalacturonan and homogalacturonan locales. They are frequently depicted in worked-on terms as the furry and smooth districts individually. Chitosan the polysaccharide is a molecule having a similar structure to cellulose with a carbohydrate backbone. It comprises two kinds of rehashing units, N-acetyl-d-

glucosamine and d-glucosamine, which are connected by β (1-4) glycosidic linkage [12-14].

Recently many researchers have taken interest in using saccharides and derivatives in the designing of TDDS [15, 16]. Cardiovascular cells are enriched with carbohydrate transporters like GLUT4 (Human Solute carrier family 2) which normally regulate glucose transportation across the cardiac cell. GLUT-4 is the fundamental iso-structure that is answerable for about 70% glucose transport across the heart cell.

Chemical grafting is a cycle by which at least one type of block is associated as a side chain to the principle chain, bringing about the development of macromolecular copolymers with changed physicochemical properties. The newly formed copolymer can be distinguished on the basis of the number, length, and molecular structure of the side chains [17].

The aim of the current study is to chemically modify the selected saccharides and then develop conjugates of Atenolol and Metoprolol with the modified saccharides for targeted delivery to the β1-receptors. These medications are generally utilized in cardiovascular arrhythmias, the executives of hypertension, myocardial dead tissue, and angina pectoris. It is expected that the targeted drug delivery of these β-blockers may increase the effectiveness of the treatment of various diseases as well as a reduction in the results of the medication.

Conclusion

Summarizing, the work of Kumbhar ST, et al. (2021) demonstrates that, the approach to enhance delivery and therapeutic outcomes of Atenolol by forming with the biodegradable and biocompatible polymeric framework is promising to improve the selectivity of medication conveyance for treatment of cardiovascular illnesses.

The current project was attempted with the primary spotlight on the advancement of active or passive targeted drug delivery systems for the better treatment of cardiovascular diseases by developing drug conjugates with the most extreme and focused on biodistribution to heart cells. The creation focused on targeted drug delivery systems include therapeutic agents, biomolecules, and carrier systems. It is needed in the future that the developed conjugates should be tested *in vivo* for confirmation of safety and efficacy in the biosystem. So the exertion taken will be valuable in the training as a possible methodology in the management of cardiovascular diseases.

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