World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:14, No:12, 2020

Double Liposomes Based Dual Drug Delivery System for Effective Eradication of Helicobacter pylori

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Abstract : The potential use of liposomes as drug carriers by i.v. injection is limited by their low stability in blood stream. Firstly, phospholipid exchange and transfer to lipoproteins, mainly HDL destabilizes and disintegrates liposomes with subsequent loss of content. To avoid the pain associated with injection and to obtain better patient compliance studies concerning various dosage forms, have been developed. Conventional liposomes (unilamellar and multilamellar) have certain drawbacks like low entrapment efficiency, stability and release of drug after single breach in external membrane, have led to the new type of liposomal systems. The challenge has been successfully met in the form of Double Liposomes (DL). DL is a recently developed type of liposome, consisting of smaller liposomes enveloped in lipid bilayers. The outer lipid layer of DL can protect inner liposomes against various enzymes, therefore DL was thought to be more effective than ordinary liposomes. This concept was also supported by in vitro release characteristics i.e. DL formation inhibited the release of drugs encapsulated in inner liposomes. DL consists of several small liposomes encapsulated in large liposomes, i.e., multivesicular vesicles (MVV), therefore, DL should be discriminated from ordinary classification of multilamellar vesicles (MLV), large unilamellar vesicles (LUV), small unilamellar vesicles (SUV). However, for these liposomes, the volume of inner phase is small and loading volume of water-soluble drugs is low. In the present study, the potential of phosphatidylethanolamine (PE) lipid anchored double liposomes (DL) to incorporate two drugs in a single system is exploited as a tool to augment the H. pylori eradication rate. Preparation of DL involves two steps, first formation of primary (inner) liposomes by thin film hydration method containing one drug, then addition of suspension of inner liposomes on thin film of lipid containing the other drug. The success of formation of DL was characterized by optical and transmission electron microscopy. Quantitation of DL-bacterial interaction was evaluated in terms of percent growth inhibition (%GI) on reference strain of H. pylori ATCC 26695. To confirm specific binding efficacy of DL to H. pylori PE surface receptor we performed an agglutination assay. Agglutination in DL treated H. pylori suspension suggested selectivity of DL towards the PE surface receptor of H. pylori. Monotherapy is generally not recommended for treatment of a H. pylori infection due to the danger of development of resistance and unacceptably low eradication rates. Therefore, combination therapy with amoxicillin trihydrate (AMOX) as anti-H. pylori agent and ranitidine bismuth citrate (RBC) as antisecretory agent were selected for the study with an expectation that this dual-drug delivery approach will exert acceptable anti-H. pylori activity.

Keywords : Helicobacter pylorI, amoxicillin trihydrate, Ranitidine Bismuth citrate, phosphatidylethanolamine, multi vesicular systems

Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development

Conference Location : Chicago, United States

Conference Dates : December 12-13, 2020