

secondary-lipophilic drug system Nano-delivery: In vitro and ex vivo studies - Raj Wagle Susbin – Curtin University

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Probuco is a highly lipophilic drug that has potent anti-inflammatory and anti-oxidant properties. It has been shown to have a protective effect on pancreatic β cells and made a potential therapeutic agent in the treatment of T2D. Despite its high efficacy and strong antioxidant effects, PB showed significant variation after oral absorption, poor oral bioavailability, and potentially severe side effects, which restricted its use. This study aimed to examine PB and LCA microcapsules in terms of the microcapsules' morphology, microcapsules membrane strength, release kinetics and biological effects *ex vivo*. Microcapsules (PB-SA and PB-LCA-SA) were prepared with a Buchi-based microencapsulating system, based on the jet-flow microencapsulation technique using polymer sodium alginate (SA) and examined *in vitro* (formulation studies) and *ex vivo*.

Both control and test microcapsules showed good and uniform morphology characteristics. Incorporation of LCA did not alter the drug content, production yield microencapsulation efficiency, zeta potential, and particle size. However, LCA reduced conductivity, microcapsules swelling, improved membrane resistance and controlled and targeted release of PB. The microcapsules swelling and drug release pattern were higher at high pH values (pH 7.8, $p < 0.05$). LCA microcapsules enhanced cell viability but not statistically significant, reduced the inflammatory profile ($p < 0.01$), increased anti-inflammatory cytokine and improved bioenergetics parameter ($p < 0.01$). LCA improved the characteristics and release pattern of PB microcapsules and also enhanced their pharmacological activity *in vitro* and *ex vivo*, suggesting potential oral targeted delivery and applications in diabetes treatment.

Introduction :

In these modern days, many significant efforts have been applied to use the potentials of lipid-based drug delivery systems, as it provides the suitable means of site specific as well as time controlled delivery of drugs with different molecular weight, either small or large, and also the bioactive agents. Poorly water-soluble drugs are challenging for the formulation scientists with reference to solubility and bioavailability. Lipid-based drug delivery systems (LBDDS) have shown the effective size dependent properties so they have attracted a lot of attention. Also LBDDS have taken the lead due to obvious advantages of upper degree of biocompatibility and versatility. These systems are commercially viable to formulate pharmaceuticals for topical, oral, pulmonary, or parenteral delivery. Lipid formulations can be modified in various ways to

meet a wide range of product requirements as per the disease condition, route of administration, and also cost product stability, toxicity, and efficacy. Lipid-based carriers are safe and efficient hence they have been proved to be attractive candidates for the formulation of pharmaceuticals, as well as vaccines, diagnostics, and nutraceuticals. Hence, lipid-based drug delivery (LBDD) systems have gained much importance in the recent years due to their ability to improve the solubility and bioavailability of drugs with poor water solubility. Routes like oral, parenteral, ocular, intranasal, dermal/transdermal, and vaginal are often for the administration of the lipid based drug delivery systems (LBDDS). However, oral route is the most preferred route because of the properties like noninvasiveness, less expensive, and less prone to side effects, such as injection-site reactions. It is also considered as the easiest and the most convenient method of drug delivery for chronic therapies. But, at a very early stage of development, formulation strategies based on a rational and systematic approach need to be developed to avoid erratic and poor *in vitro/in vivo* correlations and thus increase the chances of success in formulation development. Various useful guidelines regarding the convenient routes and formulation strategies have been published by several authors. The lipid formulation classification system (LFC) was introduced as a working model in 2000 and an extra "type" of formulation was added in 2006. In recent years the LFCs have been discussed more widely within the pharmaceutical industry to seek a consensus which can be adopted as a framework for comparing the performance of lipid-based formulations. The main purpose of the LFCs is to enable *in vivo* studies to be interpreted more readily and subsequently to facilitate the identification of the most appropriate formulations for specific drugs, that is, with reference to their physicochemical properties as depicted. The principle objective of formulation of lipid-based drugs is to reinforce their bioavailability. The use of lipids in drug delivery is no more a new trend now but is still the promising concept. Lipid-based drug delivery systems (LBDDS) are one among the emerging technologies designed to deal with challenges just like the solubility and bioavailability of poorly water-soluble drugs. Lipid-based formulations are often tailored to satisfy a good range of product requirements dictated by disease indication, route of administration, cost consideration, product stability, toxicity, and efficacy. These formulations are also a commercially viable strategy to formulate pharmaceuticals, for topical, oral, pulmonary, or parenteral delivery. In addition,

lipid-based formulations are shown to scale back the toxicity of varied drugs by changing the biodistribution of the drug faraway from sensitive organs. However, the amount of applications for lipid-based formulations has expanded because the nature and sort of active drugs under investigation became more varied. This paper mainly focuses on novel lipid-based formulations, namely, emulsions, vesicular systems, and lipid particulate systems and their subcategories also as on their prominent applications in pharmaceutical drug delivery. So far, the planning of successful lipid-based delivery systems has been based largely upon empirical experiences. Systematic physicochemical investigations of structure and stability do not only help to speed up the development of new and improved formulations, but may also aid in the understanding of the complex mechanisms governing the interaction between the lipid carriers and the living cells. Hence they sought to be safe, efficient, and specific carriers for gene and drug delivery. LBDDS are often wont to deliver various sorts of drugs from new chemical entities to newer new developments for proteins and peptides, nucleic acids (DNA, siRNA), and cellular site specific delivery. The utility of lipid-based formulations to enhance the absorption of poorly water-soluble, lipophilic drugs has been recognized for many years.