RESEARCH PROPOSAL

SYNERGISTIC EFFECT OF PAPAVERINE AND CARVEOL LOADED ZEOLITE IMIDAZOLE FRAMEWORK NANOPARTICLES FOR TARGETED DRUG DELIVERY AND CYTOTOXIC EFFECT ON BREAST CANCER

Breast cancer is the leading cause of cancer death and incidence in women across the world. According to the ICMR, India consistently reported 144,000 new cases of breast cancer and ranked third in the world for cancer rates with 68.4% annual fatality rates. Additionally, about 30% of patients survive five years after receiving a breast cancer diagnosis (Siegel, *et al.,* 2019). The effectiveness of medicinal agents is a major focus of nanomedicine. Drug delivery systems (DDSs), which typically encapsulate pharmaceutical substances, protect them against deterioration, and regulate the drug release process, considerably paved this way (De Jong, *et al.,* 2008). Metal-organic frameworks (MOFs) are a significant class of nanopores crystalline organic-inorganic materials that may be easily created from a variety of inorganic ions and organic linkers. A large surface area and porosity, simplicity of use, adaptability in size and form, inherent biodegradability, and low toxicity are only a few of their distinctive qualities (An, Jihyun, *et al.,* 2009). MOFs have recently drawn a lot of interest from biomedical community. Researchers achieved significant advancements in MOFs in this aspect to create cutting-edge drug delivery systems. Zn-based MOFs are a significant and non-toxic subclass that have been taken into consideration for use in biomedical applications (ZIFs) (Kaur, Harpeet, *et al.,* 2017). ZIF is the most researched MOF material due to its unique thermochemical stability, high loading capacity, adjustable functionality, sufficient big pore, and drug absorption and release potential (Thomas d., *et al.,* 2011). ZIF nanocarriers exhibits a pH-dependent targeted drug delivery characteristic and has capability of loading large quantity of chemotherapeutic drug against cancer (Chun-Yi, *et al.,* 2012).

The ZIF nanoparticles were synthesized by means of aqueous synthesis method of zinc nitrate and 2-methylimidazole. Then the drug was loaded and then investigated for *in-vitro* and *in-vivo* studies. Based on these grounds the following objectives are proposed:

1. The evaluation of stability and binding ability of drug molecules with the breast cancer associated protein using *in silico* techniques.
2. To synthesize and characterize the ZIF and drug-loaded (alone and in combination) of ZIF nanoparticles through SEM, TEM, EDX, XRD, FTIR, DLS and NMR analysis.
3. To evaluate effective drug loading and targeted drug release of drugs in ZIF nanaoparticles.
4. *In vitro* analysis of cytotoxicity, cell migration, apoptosis, colony formation and further protein validation using western blot.
5. Hitopathological analysis for toxicity evaluation of drugs-loaded ZIF nanoparticles treated mice.