Preface

The extract of the *Piper longum* fruit (Long pepper, Family- Piperaceae) and its phytoconstituents have been well investigated to possess anticancer activity against melanoma through *in-vitro* and *in-vivo* tumor models. Irrespective of reported anticancer activity, the poor aqueous solubility of the majority of contained phytoconstituents and the obstruction by major skin barrier, i.e., stratum corneum (SC) of skin restrict their therapeutic use through oral and transdermal routes, respectively. To improve its therapeutic properties against melanoma, two formulations, solid dispersion (SD) and transgelosome (TFG) of standardized *Piper longum* fruits ethanolic extract (PLFEE) were developed and optimized using Quality-by-Design (QbD). To maintain batch-to-batch consistency and provide dose uniformity, the PLFEE was standardized with respect to piperine (PIP) and piperlonguminine (PLGN) by high-performance liquid chromatography (HPLC). Acute oral toxicity and acute dermal toxicity of standardized PLFEE were carried out using healthy nulliparous and non-pregnant female C57BL/6 mice as per Organization for Economic Co-operation and Development (OECD) 425 and OECD 402 guidelines, respectively. The influence of various independent formulation factors on responses were statistically analyzed by response surface methodology (RSM) using 3-factor, 5 levels rotatable central composite design (CCD). The optimized SD and TFG was investigated for pharmaceutical and therapeutic activity against melanoma (B16F10) bearing C57BL/6 female mice. The anticancer activities of novel phytoformulations were also investigated with the standard anticancer drug dacarbazine (DTIC) as an adjuvant therapy. Further, the simultaneous administration of per oral SD and topical TFG formulations was carried out to investigate the *in-vivo* anticancer activity.