Polyphenolic Rich Fraction of *Physalis peruviana* Calyces and its Nanoformulation Induce Apoptosis by Caspase 3 Upregulation and G2/M Arrest in Hepatocellular Carcinoma

**Abstract**
Phytocompounds found in fruit wastes serve as nature's precious gift for humans. In this context, the present work aimed to maximize the knowledge concerning the use of *Physalis peruviana* calyces (PPC). PPC has countless health promoting phytocompounds. These phytocompounds show the privilege of being selective in their action against cancer cells without being harmful to normal cells but the precise mechanism is not understood yet. Under this scenario, we performed a detailed study to confirm that PPC and its nanoformulation can induce apoptosis both in HepG2 cells and animal models. PPC butanolic fraction (PPCBF) was prepared and tested for its total phenol, total flavonoids and HPLC analysis for phenolics, as well as the *in vitro* and *in vivo* anticancer activity for both normal and nanoforms were evaluated. The anticancer mechanisms of PPCBF and its nano form were further investigated. Results obtained revealed that PPCBF and its nano form showed high anti-HepG2 activity. Results also demonstrated that PPCBF and its nano form were able to induce Pre G1 apoptosis and cell cycle arrest (G2/M phase). Moreover, PPCBF and its nano form caused up-regulation of caspase-3 mRNA in HepG2 which could indicate that the apoptosis was mediated via the intrinsic mitochondrial pathway and the *in vivo* study confirmed these results. The therapeutic efficacy of PPCBF could be used in treating patients who are susceptible to liver function disorders. However, further detailed clinical studies are required to establish this application. Fractionation-guided evaluation could help in the development of an ideal anticancer soon. Studies are warranted to assess the potentiality of PPCBF in HCC therapy in the future. Overall, it could be concluded from this study that PPCBF and its nano form may serve as a successful and effective agents in the management of hepatocellular carcinoma (HC).

**Keywords:** Physalis peruviana, calyces, hepatocellular carcinoma, caspases, apoptosis, cell cycle arrest, rat.