

ABSTRACT

The present research intends to identify the biologically active compounds present and its synergistic effect of flavonoid and acetogenin enriched fractions of *Annona muricata* leaves and to investigate the antioxidant activity, anticancer with the focus on the antileukemic activity. The results of phase I revealed various phytochemicals present in the *Annona muricata* plant was identified using UV-Visible spectroscopy at the wavelength of 250 to 800nm. The FTIR profile revealed the presence of various secondary metabolites identified based on the functional groups. The HPTLC and HPLC analysis revealed the presence of flavonoid and acetogenin related compounds. Further, based on the peaks obtained in GC-MS analysis, the existence of diverse group of pharmacologically active compounds were confirmed. In phase II, antioxidant assessment reveals that ethanolic crude extract and all the different fraction from *Annona muricata* leaves possess radical scavenging activity against DPPH, ABTS, hydrogen peroxide and hydroxyl radicals, radical generation inhibition activity against nitric oxide and superoxide radicals, reducing power and chelating activity, among the groups tested combination group exert greater activity. In III phase, the results of anticancer activity revealed that combination treated groups possesses greater cytotoxic effect by MTT and SRB assay. In PBL treated group, there is minimal cytotoxic effect, which indicates the non-toxic nature of the *Annona muricata* leaves. Cell cycle analysis revealed that the combination treated group, were arrested at G0-G1 phase, in case of PBL, the proportion of cells were uniformly dispersed in all the phases. Annexin V-FITC/ PI staining reveals that combination treated group showed early and late apoptotic death; in case of PBL, the number of apoptotic cells were found to be very low. Mitochondrial membrane potential results reveal that combination treated group has loss of membrane integrity indicating apoptosis via intrinsic pathway and in case of normal PBL, minimal loss of MMP were seen. The evaluation of

ROS confers that *Annona muricata* ethanolic crude extract and its fractions raised up the ROS levels in Molt-3 cells and in PBL, ROS levels were not elevated. In phase IV, molecular docking studies shows that Luteolin-3', 7-di-O-glucoside (flavonoid) and Muricatacin (acetogenin) was able to interact with apoptotic targets (Mcl 1, Bcl 2, Bax), demonstrating that these compounds induced apoptosis via intrinsic apoptotic pathway and it also might be able to influence the cell signalling pathway by targeting MDM2 (Leukemia target). Therefore, it might acts as a potential source for drug development against leukemia.