Abstract

Objective: To investigate the immunomodulatory and anticancer potential of the phytoconstituents from *Brugmansia suaveolens* (*B. suaveolens*) and *Nicandra physalodes* (*N. physalodes*).

Methods: The plants from Solanaceae family have been reported to show anticancer and immunomodulatory activity. Two of the plants from this family, *B. suaveolens* and *N. physalodes*, were selected for current study. The leaves of the plants were collected and dried in shade. The ethanolic extract of both the plants were prepared using Soxhlet apparatus and fractionated using successive solvent extractions. The phytochemical characterization and bioactivity-guided fractionation using microcytotoxicity assay were carried out. The most active fractions BS3A, BS3B from *B. suaveolens* and NP3A, NP3B from *N. physalodes* were subjected to a panel of *in vivo* immunomodulatory assays using Balb/C mice. Animals were treated with the BS3A, BS3B, NP3A and NP3B (50 and 100 mg/Kg body weight) for 14 days with sheep red blood cells (SRBC) as antigen. Haemagglutination antibody (HA) titre, delayed type hypersensitivity (DTH) reaction, carbon clearance, NO production, lysosomal enzyme activity, proliferation of lymphocytes, analysis of cytokines in serum were studied. The active fractions were subjected for semi preparative HPLC to isolate the pure compounds. Isolated compounds (SUPH036-022A and SUPH036-022B) were characterized by spectral analysis. Further, SUPH036-022A and SUPH036-022B were subjected to *in vitro* immunomodulation mediated anticancer activity using co-culture assay, ROS production, mitochondrial potential assay, Cytokine estimation and cell cycle analysis.

Results: BS3A, BS3B, NP3A and NP3B showed significant *in vitro* immunostimulatory activity. The *in vivo* studies for the mentioned fractions showed significant increase in IgM and IgG antibody titre and delayed type hypersensitivity reaction (DTH) 24 and 48 h post treatment in BALB/c mice at 100 mg/Kg. Besides intensifying the humoral and cell mediated immunity, the fractions enhanced cytokine induced nitric oxide production and macrophage phagocytosis, the fractions further leading to clearance of carbon particles from reticulo-endothelial system. Moreover, a significant increase in phagocytic index, lymphocyte proliferation, lysosomal enzyme activity and cytokine levels (IL-2, IFN-γ and
IL-4) in serum were observed. Further, SUPH036-022A and SUPH036-022B were isolated from BS3B and NP3B respectively. They showed significant immunomodulation mediated breast cancer activity against MCF-7 cells. The compounds showed significant increase in the ROS production and decrease in mitochondrial potential. Both the compounds also showed increase in the IL-2 and IFN-γ production in stimulated PBMCs and significant increase in SUB-G1 phase of cell cycle in cancer cells.

**Conclusion:** The plants from Solanaceae family *B. suaveolens* and *N. physalodes* were evaluated for immunomodulatory and anticancer activity. The bioactivity guided fractionation led to selection of BS3A, BS3B from BS and NP3A, NP3B from NP respectively as immunomodulatory fractions. Further, compounds SUPH036-022A and SUPH036-022B were isolated from BS3B and NP3B respectively, showed potent anticancer activity through stimulation of immune system. The compounds should be explored further as potential anticancer agent.