Abstract
1. **ABSTRACT**

The present study was designed to carry out macroscopic and microscopic study of fruit of *Benincasa hispida* (Thunb.) Cogn (Cucurbitaceae) along with evaluation of multiple pharmacological activities to elucidate its mechanism of action. These activities includes evaluation of in-vitro antioxidant activity then anti depressant activity, anxiolytic activity, anti-psychotic activity, anticonvulsant activity, nootropic activity, antiulcer activity, anti-inflammatory activity, analgesic activity and immunomodulatory activity.

The macroscopy and microscopy studies were carried out to authenticate the fruit of *Benincasa hispida* (Thunb.) Cogn (Cucurbitaceae). The fruit in transverse section showed epicarp, mesocarp with stone cells, sclereids, phloem and xylem fibers. The macroscopy and the microscopy study revealed the authenticity of the fruit of *Benincasa hispida*.

Preliminary phytochemical screening revealed the presence of phytoconstituents like amino acids, flavonoids, terpenes and steroids in the fruit of *Benincasa hispida*. The preliminary screening using TLC technique reflected the presence of phytoconstituents viz. beta-sitosterol and lupeol in petroleum ether extract and iso-vitexin and amino acids in methanolic extract. Further, quantitative HPTLC was carried out, which revealed the presence of 6.52 % of beta-sitosterol and 2.48 % of lupeol in petroleum ether extract.

We have also studied different pharmacological activities of petroleum ether, methanolic, ethyl acetate and aqueous extract of fruit of *Benincasa hispida* using various experimental models.
The in-vitro antioxidant study of methanolic extract was carried out by checking free radical scavenging (using DPPH), superoxide scavenging, lipid peroxidation, hydroxyl radical scavenging, erythrocyte membrane stabilizing and nitric oxide scavenging activity. Out of all these, methanolic extract showed mild to moderate antioxidant effects against free radical scavenging, superoxide scavenging, lipid peroxidation and hydroxyl radical scavenging activities. While no significant effect against erythrocyte membrane is stabilizing and nitric oxide scavenging activity.

Methanolic extract (300 mg/kg and 1000 mg/kg, p.o.) was evaluated for its multiple pharmacological effects on CNS viz. antidepressant (behavior despair test), anxiolytics (elevates plus maze and open field behavior), anticonvulsants (Maximal electric shock method), antipsychotic (D-amphetamine induced stereotype and cox’s pole climbing apparatus) and Nootropic effect. Methanolic extract possessed mild to moderate all above listed activities except antidepressant activity.

The antiulcer activity was evaluated using different models viz. ethanol-induced gastric mucosal damage, pylorus ligated (PL), cold restraint-stress (CRS)-induced ulcer, ethanol-induced and indomethacin pretreated model, ethanol-induced and N-ethyl maleimide (NEM) pretreated model, ethanol-induced and N- nitro-L-arginine methyl ester (L-NAME) pretreated model in rats. In all the models Petroleum ether and methanolic extracts were administrated orally at the dose of 300 mg/kg, while omeprazole (reference standard) at the dose of 20 mg/kg, orally. Further, in ethanol-induced mucosal damage model, ethyl acetate (300 mg/kg, p.o.) and aqueous extract (300 mg/kg, p.o.) were also tested.
Ulcer index was the common evaluating parameter in all the models. In PL-model different biochemical parameters were also tested. Additionally antioxidant potential was evaluated by finding out the level of lipid peroxidation (LPO), superoxide dismutase (SOD) and catalase (CAT) in case of CRS-induced ulcer model. Statistical analysis of data was done using one way ANOVA followed by Tukey's multiple range tests (p<0.05 was considered as significance limit).

Both petroleum ether and methanolic extract showed significant (p<0.05) reduction in ulcer index in ethanol-induced gastric mucosal damage, PL-induced ulcer and CRS-induced ulcer models. In biochemical investigations, methanolic extract showed significant (p<0.05) decrease in volume of acid secretion, increase in pH, while both the extract treated animal showed significant (p<0.05) reduction in pepsin activity as compared to the control group. Further, both the extract showed increase in carbohydrate content and increase in TC:PR ratio (mucin activity). In case of CRS-induced ulcer model both the extract showed significant (p<0.05) reduction in lipid peroxidation and significant (p<0.05) increase in catalase level. However, there was no statistical significant difference observed in the level of superoxide dismutase (SOD).

In case of ethanol-induced and indomethacin pretreated as well as NEM and L-NAME pretreated models, both petroleum ether and methanolic extract showed no significant reduction in ulcer index, which indicates there was a role of endogenous prostaglandins, sulphydryls and nitric oxide in the protective effect against ethanol-induced gastric mucosal damage.
The petroleum ether and methanolic extracts (300 mg/kg, p.o.) were tested for anti-inflammatory activity using carrageenan and histamine-induced acute inflammation and cotton pellet-induced chronic inflammation. Both the extract showed significant reduction (p<0.05) in paw volume in case of acute inflammation while no significant reduction in case of cotton pellet-induced chronic inflammation.

Analgesic activity of petroleum ether and methanolic extracts (300 mg/kg, p.o.) were studied using acetic acid-induced writhing, formaline induced biting and tail flick test. Out of these three models, both the extract showed significant (p<0.05) protection in case of acetic acid-induced writhing and formaline induced biting response while no significant (p>0.05) protection in tail flick test. These results indicates that both the extract had only peripheral analgesic effect and devoid of central analgesic activity.

Immunomodulatory activity was tested by using different models viz. sheep RBC induced HA titre and DTH response, and then hematological study and cyclophosphamide induce myelosuppression. Both petroleum ether and methanolic extracts (100 mg/kg and 300 mg/kg, p.o., respectively) showed no significant (p>0.05) effect on sheep RBC induced HA titre and DTH response, and hematological profile. But methanolic extract showed significant (p<0.05) protection against cyclophosphamide induce myelosuppression. This result indicates that methanolic extract had no direct immunostimulant effect rather it prevent immunosuppressive effect of cyclophosphamide by some indirect effect.
Abstract

It can be concluded from our study that methanolic extract of *Benincasa hispida* (Thunb.) *Cogn* possessed significant in-vitro antioxidant, anxiolytic, anticonvulsant, antipsychotic, Nootropic effects and mild immunostimulant effects. Further, methanolic and petroleum ether extracts showed significant (p<0.05) antiulcer, in-vivo antioxidant property, anti-inflammatory and analgesic activity by significant reduction in UI and in lipid peroxidation level along with significant increase in CAT level.