10-SUMMARY
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Total alcoholic extract (WO-1), total alkaloids (WO-2), aqueous extract (WO-3) of fruits of *Withania coagulans* Dunal and a withanolide (WO-4) isolated from the fruits have been screened pharmacologically especially for their effects on CNS, CVS and anti-inflammatory activity. A brief account of the effects observed is as under:

1. WO-1, WO-2 and WO-3 at 1 gm/kg, 200 mg/kg and 5 ml/100 gm of body weight respectively had mild depressant effect on central nervous system in rats of either sex. There was prolongation of pentobarbitone induced hypnosis. These exacerbated the convulsions produced by metrazol and electro-shock seizures in rats. All the extracts increased the metrazol and amphetamine toxicity but did not show any narcotic type of analgesic activity in rats. WO-1 and WO-2 reduced the fright response in rats induced by auditory stimulus. Total alkaloids appear to be more than 5 times active than alcoholic extract. WO-1 up to a dose of 10 gm/kg and WO-2 up to a dose of 6.4 gm/kg orally were found to be non-lethal in rats.
WO-4 did not show any effect on CNS when administered to rats by i.p. route. However, when administered i.v. through tail vein at 30 mg/kg it produced mild depression. There was no lethal effect in mice up to 625 mg/kg i.p.

3. WO-1, WO-2 and WO-4 at doses of 1 gm/kg, 200 mg/kg and 10 mg/kg body wt. respectively produced significant anti-inflammatory effect in subacute inflammation induced with formalin and granulation tissue formation with cotton pellets. On weight basis the withanolide was found to be about 5 times more active than phenylbutazone and almost equipotent to hydrocortisone. Since the withanolide is almost as active as hydrocortisone and its concentration in fruits is about 30 mg%, the anti-inflammatory effect of the fruits can be attributed to this withanolide. The withanolide is about 100 times more active than alcoholic extract.

3a) WO-1 and WO-2 at 50-100 mg/kg and 20 mg/kg respectively produced immediate transient fall of blood pressure, returning to normal followed by sustained moderate fall (26.0±6.3 mmHg and 27.4±5.2 mmHg respectively), and bradycardia and respiratory
stimulant effect in anaesthetised dogs. The fall of blood pressure was recorded in rabbits and rats too. The hypotensive effect, especially the initial transient fall seems to be mainly due to direct depressant effect on the myocardium as the effect was not blocked by atropine, propranolol, mepyr-amine, hexamethonium bromide or indomethacin in usual doses. The depressant effects in perfused frog heart, rabbit Langendorff preparation and ECG studies further support this contention. A reduction in perfusion fluid was observed with these preparations in rats hind limb preparation. Phytochemical together with pharmacological studies revealed that water soluble alkaloids were responsible mainly for immediate transient fall in blood pressure and water insoluble alkaloids for sustained hypotensive response.

b) The withanolide at 5 mg/kg body wt. produced moderate fall of blood pressure in dogs (34±2.1 mmHg) which was blocked by atropine and not by mepyr-amine or propranolol. In rabbit Langendorff preparation and ECG studies it produced myocardial depressant effect but in perfused frog heart it produced mild positive inotropic and chronotropic response.
4. With WO-1, WO-2 or WO-3, decreased urine output was observed in rats.

5. WO-4 and WO-3 at 10 mg/kg and 5 ml/100 gm dose respectively produced significant protection of CCl₄ induced acute hepatotoxicity. The protective effect was observed by decrease of pentobarbitone induced hypnosis, reduction in SGPT and SGOT levels and histopathological examination of liver tissues.

6. The withanolide did not show any antitumor activity when tested in mice against P388 lymphocytic leukemia.

7. Mild antibacterial activity was observed with the withanolide when tested against standard strains of E. coli and Staph. aureus.

8. Total alkaloids and water soluble portion of alcoholic extract produced non-specific relaxant effect on various smooth muscles of the common laboratory animals. However, extracts had vasoconstrictor effect when tested on rat hind limb preparation.
9. In general, the pharmacological effects of *W. ashwagandha* Kaul, *W. coagulans* Dunal and *W. somnifera* Dunal on CNS, CVS and inflammation are qualitatively similar and the active principles isolated from all these plants are alkaloids and withanolides.