SUMMARY AND CONCLUSIONS
Gold is used only for the treatment of rheumatoid arthritis in modern medicine. Calcined gold preparations used in Indian Systems of Medicine are, however, valued for varied pharmacodynamic properties and therapeutic effects including general tonic, hepatotonic, cardiostimulant, nervine tonic, aphrodisiac, detoxicant, anti-infective, rejuvenating and anti-ageing action. In this study Ayurvedic Swarna Bhasma (SB), Unani Kushta Tila Kalan (KTK) and modern Auranofin (AN) were subjected to more than 30 tests for general neuropsychopharmacological effects, cognitive functions, antidepressant, anxiolytic, neuroleptic, serenic, growth promoting, anti-fatigue, glycogen sparing, adaptogenic and immunomodulatory effects. The test drugs were also investigated for effects on varied enzymatic parameters and neurotransmitters and also for safety aspects.

The gold preparations (KTK, SB, AN) exhibited good analgesic activity against chemical, electrical, thermal and mechanical noxious stimuli in rats and mice. The effects were found to be dose-dependent (except for AN) and compared well with standard drug morphine and acetylsalicylic acid (ED50 values for SB and KTK: approx. 20 mg/kg). The effects of KTK and SB were partly blocked by naloxone suggesting possible involvement of opioid receptors in their mechanism of analgesic action.

All of the test drugs exhibited marked anti-cataleptic actions (which compared well with standard drug L-DOPA) and elevated DA concentration in various regions of brain. These findings suggest therapeutic potential of gold preparations in Parkinson’s disease through favourable effects on dopaminergic system.
All gold preparations elicited nootropic effects in both active and passive avoidance models in rats and mice. The test drugs also caused reduction in AChE activity in frontal cortex and hippocampus which lead to increased ACh level in brain thus causing improvement in learning and memory. Increase was also observed in NE and DA levels in various regions of brain. Precise mechanism of action for nootropic effects remains to be elucidated.

The test drugs (KTK, SB and AN) showed interesting anti-depressant and anxiolytic activity. The drugs caused decreased immobility time in forced swimming test and reversed the increase in shock-induced escape failures in the learned helplessness test. A significant increase in punished drinking episodes in anxiometer, more open arm entries and time spent in plus maze and reduction in behavioural deficit was observed. The increase in 5-HT levels, seen after treatment with gold preparations, could play an important role in probable mechanism of anti-depressant and anxiolytic actions of the test drugs. Facilitation of central dopaminergic action may also contribute to such effects.

The gold preparations (SB and KTK) revealed interesting anti-aggressive actions against isolation, electroshock and apomorphine-induced aggressive behaviour in rats and mice. These effects were possibly elicited through normalization of serotonergic circuits. AN failed to elicit such effects.

The test drugs (KTK, SB) restored exercise-depleted liver and muscle glycogen and adrenal cholesterol level indicating carbohydrate-sparing and anti-fatigue effects. The
effects comparable well with *Panax ginseng*: a reputed adaptogen and rejuvenating plant drug. AN failed to elicit such effect.

Supplementation of the test drugs into the diet (0.01% w/w) of growing rat pups showed increase in growth rate. KTK and SB showed better efficacy as compared to AN. These effects may be attributed to better utilization of amino acids and protein synthesis.

The calcined gold preparations (KTK and SB) revealed favourable actions on non-specific resistance of the body (adaptogenic action) as evidenced by normalization of milk-induced leucocytosis. The results compared well with *Panax ginseng*. AN showed no adaptogenic effect.

AN showed immunosuppressive effects, calcined gold preparations (KTK and SB) elicited immunostimulating effects. The test drugs (KTK and SB) revealed no toxicity on vital tissues like liver, kidney, spleen and thymus histology; slight manifestations were noted at higher doses. The calcined gold preparations showed modulatory response in both cellular and humoral immunity as evidenced by significant increase in cellularity counts of lymphoid organs and macrophages, enhancement of plaque-forming cells and increase in foot pad thickness. AN treatment elicited reduction in peritoneal macrophages and lymphoid cell counts, plaque forming cell (PFC). The test drugs (KTK and SB) also revealed significant and dose-dependent stimulation of phagocytosis as evidenced by increase in phagocytic index and phagocytic capacity. AN, on the other hand, showed inhibitory action on phagocytosis. The calcined forms showed significant inhibitory
effect against Ehrlich's ascites tumour challenge. Further the onset of tumour formation was delayed in treated animals.

11. All of the gold preparations under study (KTK, SB and AN) revealed encouraging antioxidant and anti-lipidperoxidative activity as evidenced by significant enhancement of anti-oxidant enzymes viz. catalase, GST, GSH, GPD and GR. The test drugs decreased the rate of lipid peroxidation in liver and brain; KTK showed protection only in brain tissue.

12. None of the test drugs (KTK, SB and AN) elicited any effect on gross behaviour, abnormalities in posture, respiration, catalepsy, piloerection, salivation, hyperactivity, stereotypy; ptosis, size of pupils, cyanosis, lacrymation, sweating, diarrhoea, loss of reflexes following single does up to 1-2 g/kg for KTK and SB and 200 mg/kg for AN. The test drugs did not elicit any effect on spontaneous motor activity (traction test, photoactometer), endurance (activity wheel), rectal temperature (normal and yeast pyretic rats), appreciable anti- or pro-convulsant effects (PTZ, MES, strychnine-induced seizures in mice) and exercise depleted adrenal ascorbic acid levels. AN failed to show anti-aggressive, adaptogenic and glycogen-sparing effects elicited by calcined gold preparations KTK and SB.

3. Most of the effects were observed at 25 mg/kg po for KTK and SB and 2.5 mg/kg for AN. The MTD for KTK and SB were found to be > 2 g/kg, po (40-80 x ED) and > 100mg/kg, po for AN (20-40 X ED) indicating wide margin of safety. The test drugs
revealed no ill effects on other CNS parameters e.g. spontaneous motor activity, conditioned and unconditioned avoidance response, motor deficit or rota rod fall out indicating lack of subtle toxic effects. No hematological abnormalities were seen following 10 days treatment with KTK and SB (25 and 50 mg/kg) and AN (2.5 mg/kg). Instead of weight loss or immunosuppression, growth promotion and immunostimulation was observed in treated animals. While long-term toxicity studies have not been done, present results indicate wide range of safety for the test drugs.

14. Heavy metals including calcined gold preparations under study, hitherto known only for their negative aspects, revealed interesting analgesic, anti-cataleptic, nootropic, antidepressant, anxiolytic, anti-aggressive, adaptogenic, antioxidant and immunomodulatory effects. These findings are being reported for the first time in the gold preparations used in both traditional and modern systems of medicine. The test drugs exhibited an overall improvement in physical (growth promotion, anti-fatigue) and mental (analgesic, nootropic, anti-cataleptic, anxiolytic and anti-depressant) performance and ability to cope up with stress, toxicity and infection (anti-oxidant, adaptogenic and immunomodulatory effects) without discernible gross or subtle toxic effects. Research in this area did not receive requisite scientific attention because of undue apprehension about the hazardous effects of metals. A dispassionate approach is needed to unearth their therapeutic potential. The test drugs are not pure compounds and owe their efficacy and safety to the formation of unidentified complexes of gold with herbal ingredients during the ashing process. These aspects and mechanisms involve warrant further investigations.


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