EVALUATION OF STANDARDIZED EXTRACT OF CENTELLA ASCIATICA LEAVES ON SUICIDAL BEHAVIOR-RELATED TRAITS IN LABORATORY RATS

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Introduction
Depression can be long-lasting or recurrent, substantially impairing an individual’s ability to function at work or cope with daily life (1). At its most severe, depression can lead to suicide (2).
Serious risks involved with antidepressants especially fluoxetine can induce or exacerbate suicidal tendencies is still debated (3-4).
Social isolation (an animal model of stress) may enhance anxiety in rats after 7 days of isolation. The non-physical nature of social isolation minimizes discomfort yet reveals stress responses in animals, which stimulate the HPA axis activity as has been shown in other stress paradigms (5-7).
Asiaticoside (AS) is a major pentacyclic triterpenoid saponin of Centella asiatica L with antidepressant (8) and anxiolytic (9) effects. We reported ‘Standardized extract of Centella asiatica L (INDCA) act by ameliorating HPA axis and by augmenting the expression of brain 5HT1A receptors’ (10).

Materials and Methods

Animals: Male Sprague-Dawley rats Protocol was approved by Institutional Animal Ethics Committee (IAEC), SIOP.

The purity of asiaticoside in INDCA was found to have 45.74% (10)

High-performance liquid chromatography (HPLC) of (A) INDCA standardized to asiaticoside (C2) at RT = 8.233 min (B) reference standard (asiaticoside) at RT = 8.242.

Socially isolated for 14 days

Suicidal behavior traits

Resident Intruder paradigm: Aggression
• Attack bites
• Tail rattling
• Wrestling
• Chasing behavior
• Attack latency

Active avoidance learned helplessness:
• irritability:
• Reactivity to stimuli
• Escape latency
• Escape failure

Parameters were recorded on day 1, 7 and 14 of isolation

Biochemical estimation
Estimation of plasma cortisol

Discussion and Conclusion
Suicide is a complex behavior which is impossible to fully reproduce in an animal model.
Traits linked with suicide in humans can be successfully modeled in rodents that include aggression, impulsivity, irritability and hopelessness/helplessness (11).
High levels of aggression is the risk factor of suicide (12). INDCA exhibited the anti-aggressive effects as evident by number of bites, tail rattling and reduction in attack latency more than that of fluoxetine. Chronic treatment with SSRI are reported to aggravate aggression (13).
Many studies report that irritability is strongly associated with suicidal ideation and suicide attempts (14). INDCA but not fluoxetine prevented it.
Helplessness means pessimism which prominently correlates with suicide clinically as observed in controlled animals. INDCA dose dependently but not fluoxetine treatment showed reduced escape latency and escape failure. The present study are in correspondence with the previous results (15).
HPA hyperactivity is associated both with non-fatal suicidal behavior and completed suicide. Hypothalamus, a major controlling center of the HPA axis, is important target of glucocorticoids/cortisol.
Fluoxetine treatment showed significant increase in plasma cortisol whereas INDCA treatment reduced it dose dependently.
Fluoxetine or other SSRIs, treat depression but do not take care of suicidal tendency due to HPA axis hyperactivity. The protective effect of INDCA is arbitrated due to regulation of HPA axis function as reported previously by us (10).

References