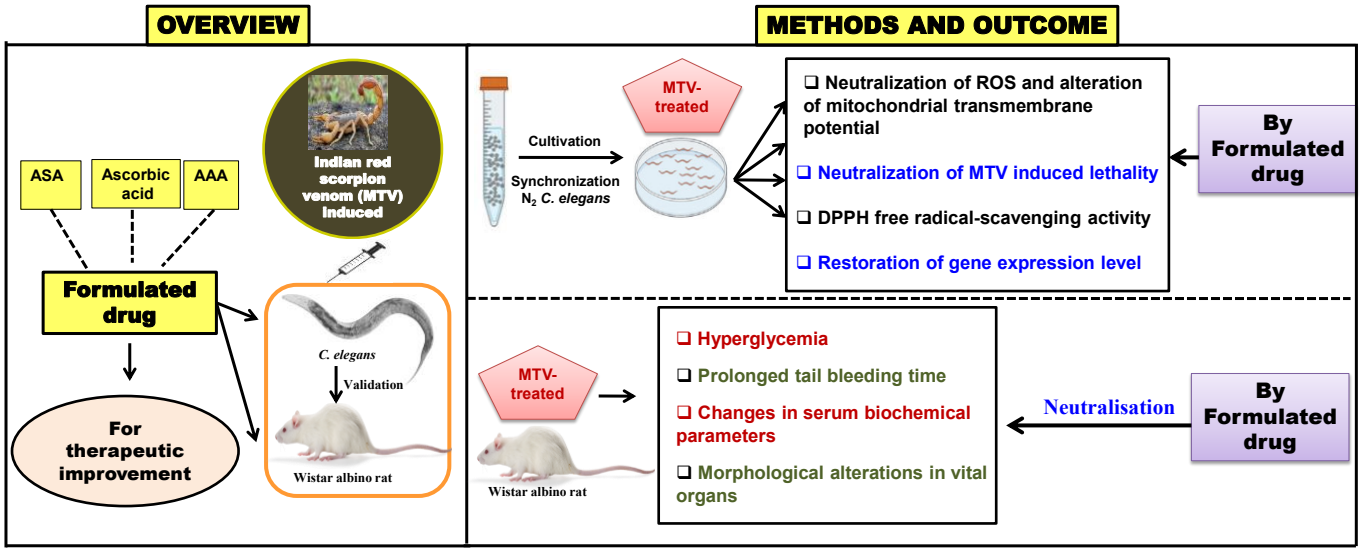
Technology developed for patent

i) **Name of the Technology:** "A Pharmaceutical composition for the Treatment of Indian Red Scorpion Venom (*Mesobuthus tamulus*) Induced Toxicity.

ii) **One graphical image:**



iii) **Brief description of the technology:**

The present invention relates to the invention of a drug composition comprising of commercial ASA, ascorbic acid and α1-adrenoreceptor antagonist, which is capable of neutralizing the in vivo toxic effect of *M. tamulus* venom in *C. elegans* and Wistar strain albino rats.

iv) **Details about the technology:**

The present invention relates to the invention of a drug composition comprising of commercial ASA, ascorbic acid and α1-adrenoreceptor antagonist, which is capable of neutralizing the in vivo toxic effect of *M. tamulus* venom in *C. elegans* and Wistar strain albino rats.

In high-throughput methods like drug screenings and therapeutic target discovery, *Caenorhabditis elegans*, a nematode, has been successfully employed to recapitulate a variety of human illnesses at the molecular level. *C. elegans* also acts as a model for assessing neurotoxicity and thus an alternative model to mammalian systems.

The LD_{50} doses of *M. tamulus* venom in Swiss albino mice and Charles foster rats were determined by known method. The LD_{50} dose of *M. tamulus* venom (i.v.) in anaesthetized adult rats (Charles Foster strain) was determined as 95 ± 13.2 µg/kg weight, whereas in Swiss albino mice, the LD_{50} dose (i.v) was reported as 7.2 ± 1.35 mg/kg which is significantly greater than the LD_{50} value in Charles Foster strain rat. Therefore, first MTV neutralization potency of formulated drug composition was tested and individual components of the composition in *C. elegans* was used to save the experimental animals. This was done followed by determining the MTV toxicity neutralizing potency of formulated drug composition in experimental animals (albino Wistar strain rat).

The novel formulated drug composition comprising commercial ASA (obtained from Premium serum and Vaccines Pvt Ltd, Pune, India), α1-adrenoreceptor antagonist e.g. Prazosin, Silodosin, and ascorbic acid is capable of efficient in vivo neutralization of MTV-induced toxicity in *C. elegans* followed by albino Wistar strain rats. The results obtained are surprising better than the individual components of the composition. Not only the novel composition of the present invention is more efficacious in treating the MTV related issues but also the composition can effectively overcome the inherent side effects associated with the conventional treatment by ASA and/or α1-adrenoreceptor antagonists e.g. Prazosin, Silodosin, as is prevalent today. Accordingly, this novel composition is a very promising candidate to pave the way for the significant improvement of efficient in-patient management of scorpion stings.

The components of formulated drug composition (commercial ASA: α1-adrenoreceptor antagonist: ascorbic acid) act synergistically to neutralize the MTV-induced toxicity. *The* pre-clinical assessment for assessing the efficacy of antivenom and other drugs serves as a gold standard by determining their neutralization potency against scorpion venom-induced toxicity.

The invention shows that the formulated drug composition act synergistically to reduce these toxic effects of MTV produced free-radicals and altered mitochondrial transmembrane potential on *C. elegans.*

MTV showed hyperglycaemia in Wistar strain albino rats within 30 min-60 min post-treatment. Besides, α1-adrenoreceptor antagonist at higher concentration was also reported to induce hyperglycaemia. Histological manifestations such as tissue necrosis, edema, muscle damage was observed in MTV induced rat tissue namely heart, kidney, liver and lung and their morphological alteration was also examined when treated with formulation drug compositions. Moreover, molecular mechanism was also studied where *M. tamulus* venom significantly upregulated the genes involved in apoptosis, detoxification and stress response. Therefore, this formulated drug composition was used to evaluate its efficacy in the neutralization of MTV-induced toxicity in *vivo C. elegans* and rat model. Both the models demonstrated significantly improved neutralization efficiency of formulated drug composition as compared to its individual component against *M. tamulus* venom-induced toxicity.

In the present invention three sets of pharmaceutical composition comprising commercial Anti-Scorpion Antibody (ASA), ascorbic acid and anα1-adrenoreceptor antagonist in a w/w ratio of-

(i) ASA (93.75 µg): ascorbic acid (0.05 µg): α1-adrenoreceptor antagonist (1.5 µM)- Composition 1;

(ii) ASA (187.5 µg): ascorbic acid (0.1 µg): α1-adrenoreceptor antagonist (3 µM)- Composition 2; and

(iii) ASA (375 µg): ascorbic acid (0.2 µg): α1-adrenoreceptor antagonist (6 µM)- Composition 3, were prepared and tested, which are described in detail below.

In an embodiment the process for preparation of the pharmaceutical composition of the present invention comprises the steps of providing commercial Anti-Scorpion Antibody (ASA), ascorbic acid and anα1-adrenoreceptor antagonist; dissolving the commercial Anti-Scorpion Antibody (ASA), ascorbic acid and α1-adrenoreceptor antagonist in water and 1X PBS as buffer; to provide the composition in a w/w ratio selected from

(i) ASA (93.75 µg) : ascorbic acid (0.05 µg) : α1-adrenoreceptor antagonist (1.5 µM);

(ii) ASA (187.5 µg) : ascorbic acid (0.1 µg) : α1-adrenoreceptor antagonist (3 µM); and

(iii) ASA (375 µg): ascorbic acid (0.2 µg): α1-adrenoreceptor antagonist (6 µM).

The invention shows that the formulated drug composition act synergistically to reduce these toxic effects of MTV toxicity on *C. elegans* and Wistar strain rats.

v) What problem was solved or applicability of the technology:

The present invention relates to a pharmaceutical composition for the treatment of Indian red scorpion venom induced toxicity. Particularly, the present invention relates to a pharmaceutical composition, comprising commercial anti-scorpion antivenom (ASA), an α1-adrenoreceptor antagonist and ascorbic acid that act synergistically to neutralize the Indian red scorpion (*Mesobuthus tamulus*) venom-induced toxicity to a significantly greater extent as compared to conventional treatment.

vi) Patent status:

Patent has been granted on 13/01/2025

vii) Contact details of the concerned scientist for further information:

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