

## Unlocking the anticoagulant potential of Barrel Jellyfish tentacle extract

Cnidarians in spite of their toxicity have long been indicated as a potential source of natural bioactive compounds of pharmacological concern useful to develop new drugs or biomedical materials. A number of metabolites, anti-cancer, anti-microbial and anti-oxidant compounds have been isolated in the interest of human health and have been found to be active at the cellular level and this makes them possible sources of new drugs.

Thrombosis and related cardiovascular disorders are major life threatening diseases of mankind. Currently used drugs to counter these disease conditions have various limitations including uncontrolled activity leading to haemorrhage or lower efficacy and sometimes, allergic reactions. These limitations drive the continual and intense efforts to develop new anticoagulants targeting specific coagulation factors. Several snake venom-derived toxins and hematophagous animal toxins have shown strong anticoagulant properties. Many of these toxins can dissolve blood clots at very low dose. Search for the ideal anticoagulant with minimal side effects have become a challenging field for the researchers.

This study was aimed at the assessment of anticoagulant and platelet aggregation inhibiting activities in the tentacle extract of one of the commonly found jellyfish species on the Goan coast i.e. Barrel jellyfish (*Rhizostomapulmo*). The tentacle extract was capable of inhibiting the blood coagulation cascade at three different levels: 1) Platelet aggregation 2) Fibrinogen digestion 3) Fibrin degradation.

Barrel jellyfish tentacle extract (BJFTE) could digest fibrinogen in dose and time dependent manner. It could digest clots, made with fibrinogen but not the ones made with essentially plasminogen free fibrinogen suggestive of the fact that there is possible correlation between plasminogen and BJFTE with respect to fibrin clot digestion. Fibrinogenolytic and fibrinolytic activities of BJFTE were significantly reduced in presence of EDTA and on pre-exposure to heat, but not on pre-treatment with PMSF. This observation indicated the involvement of thermolabile metalloproteinases in the above-mentioned activities. BJFTE showed dose and time dependent hemolytic activity against human RBCs. The RBCs on exposure to BJFTE initially showed swelling of the cells followed by gradual crenation. It lacked phospholipase activity and could also inhibit ADP dependent platelet aggregation in a dose dependent manner. BJFTE exhibited strong proteolytic activity on fibrinogen, casein, gelatin and azocasein, which was significantly lost on treatment with EDTA.

Owing to the highly unstable and aggregation prone nature of the jellyfish proteins, various attempts were made using combinations of purification techniques to purify active protein/peptides from BJFTE. As a result of a combination of ammonium sulphate precipitation and SE-HPLC, a semi-pure anticoagulant fraction was obtained, which showed strong fibrinogenolytic activity but no

fibrinolytic activity. A 95 kDa metalloproteinase was identified in this fraction and was named Rhizoprotease. Atomic absorption spectroscopy studies suggested the presence of  $Zn^{+2}$  in BJFTE as well as in the semi-pure fraction containing Rhizoprotease. Protein mass fingerprinting analysis revealed that Rhizoprotease is a novel protein and was found to have similarity with invertebrates like *Dinoponera quadriceps* (giant ant), *Taeniasaginata* (beef tapeworm), *Helobdella robusta* (freshwater jawless leech), *Lepeoptheirus salmonis* (hookworm), *Ancyclostomaceylanicum* (sea louse), *Aedes albopictus* (mosquito). All these invertebrates are known to have anticoagulant and antiplatelet activities. These results suggest that Rhizoprotease has some sequences similar to several anticoagulant proteins of invertebrate origins.

This work reveals, for the first time, the anticoagulant potential of jellyfish tentacle extract. It also details a novel anticoagulant metalloproteinase, Rhizoprotease from *Rhizostoma pulmo*. The work presented here increases the bio-discovery potential of jellyfish and provides direction for future research to consider them as a source for designing anticoagulant/antiplatelet/thrombolytic drugs.

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## **Publication**

[Partial purification and identification of a metalloproteinase with anticoagulant activity from \*Rhizostoma pulmo\* \(Barrel Jellyfish\).](#)

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