Notification No: 564/2024

Date of PhD Award: 07-08-2024

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Topic of Research: "Spectroscopic studies on interaction of potential phytotherapeutic with selected proteins"

Key Findings

Candida and *Aspergillus* are major groups of fungi that are responsible for serious infections such as Candidiasis and Aspergillosis. Although numerous antifungal drugs have been developed, additional new therapies are needed, due to the established emergent resistant strains against the available drugs and high toxicity of current treatments, placing substantial health and economic burdens on patients. Currently, antifungal treatments are primarily limited to four major classes—fluoropyrimidine analogues, polyenes, azoles, and echinocandins—which target just three key metabolic pathways in fungi. Other groups of antifungals are used topically, like morpholines and allylamines, because of the inability of the systemic and the accompanying side effects. Even though the targets of ancient antifungals are the membrane and wall of the fungal cell, new targets like nucleic acid synthesis, accessory protein, heat shock protein 90, ergosterol biosynthesis, cellular cell efflux mechanisms, and bacterial mitochondria have come up in recent research.

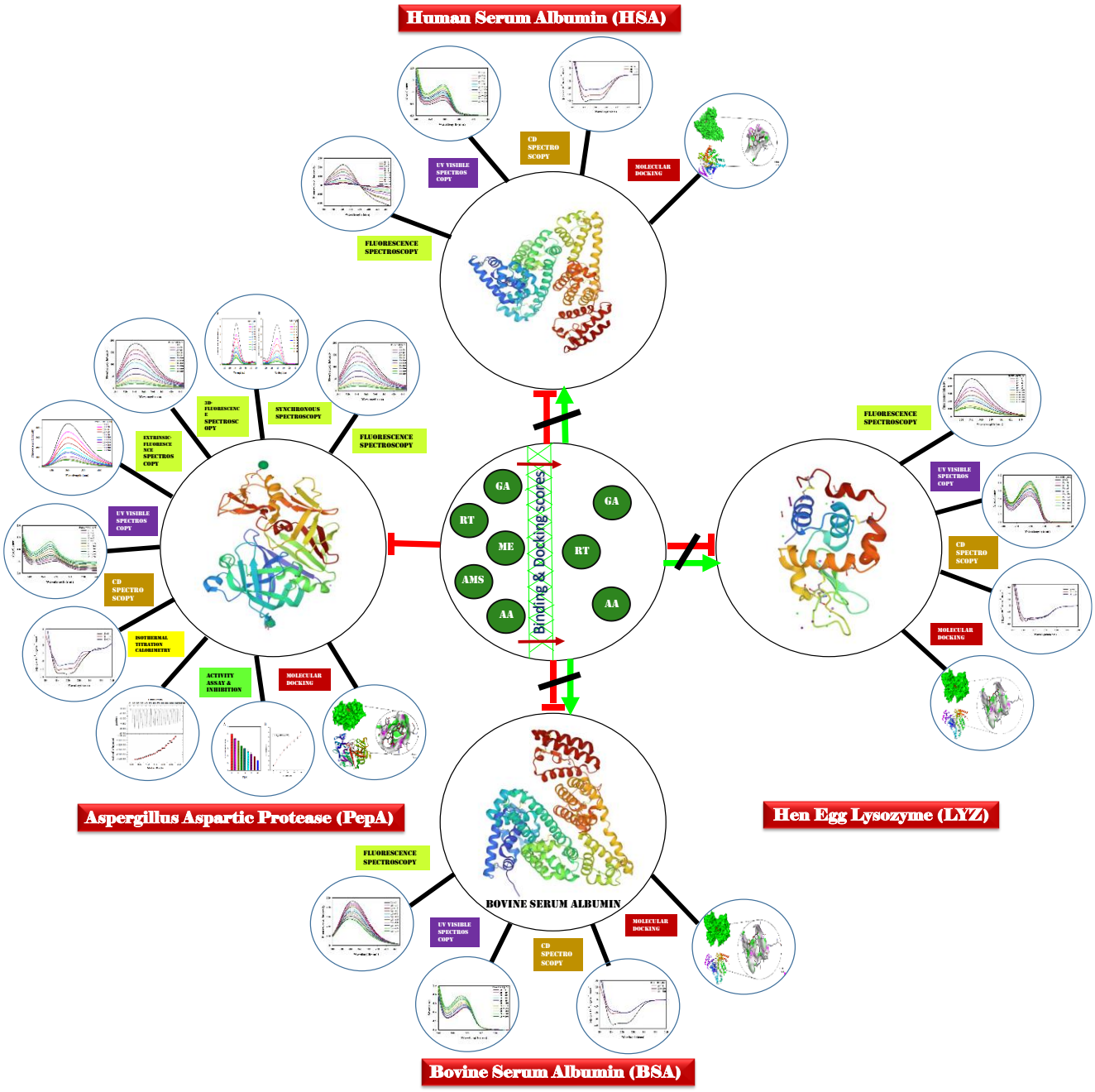
In this research study, we suggest plant-based natural compounds as a source of the alternative use of medicine for fungal infections. It looks into the anti-fungal properties of substances such as gallic acid (GA), rutin (RT), methyl eugenol (ME), allyl methyl sulfide (AMS), and p-allylanisole (AA) against

Aspergillopepsin-1 (PepA). The study therefore assessed binding and inhibitory potential of these compounds against PepA using spectroscopic and computational methods; similarly, the results were compared to their interactions with human serum albumin, bovine serum albumin, and lysozyme in order to perform an estimation for binding efficiency and potential applications on systemic studies.

The research found that RT and GA are strong inhibitors of PepA, showing significant binding affinity and structural disruption, with 50% inhibition at concentrations of 132.41 μmoles/L and 114.12 μmoles/L, respectively. In contrast, ME and AMS exhibited lower binding energies and were less effective. Fluorescence spectroscopy and molecular docking studies confirmed the order of binding affinity as GA > RT > AA > ME > AMS, with RT showing the highest binding energy of -10 kcal/mol. Molecular dynamics (MD) simulations suggested that GA, RT, and AA significantly destabilize the PepA structure, exposing more hydrophobic residues.

The study was further supported by an acceptance ratio in comparative studies on HSA, BSA, and lysozyme: significant binding of RT, GA, and AA without causing important structural changes. It was definitely observed that significant binding took place with high affinity with HSA and BSA when treated with RT, together with strong stabilization when compared with lysozyme. The lysozyme affinity order was RT > GA > AA. Docking studies reinforced these findings, with RT emerging as the most effective binder and stabilizer of these proteins.

In conclusion we find that among all the identified compounds, GA and RT were revealed as the two most active antiprotease compounds showing activity against both human and bovine systems, while most of the native confirmation of the proteins HSA, BSA, and lysozyme is retained. These data suggest that natural compounds isolated from plants, specifically GA and RT, hold promise as a new effective modality in the treatment of invasive fungal infections.



Graphical representation of the key findings of the thesis: Spectroscopic studies on interaction of potential phytotherapeutic with selected proteins