Synergistic Interaction of Important Phytochemicals With Human Serum Albumin (HSA)

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Background and Significance

HSA is the major protein carrier in the human bloodstream and accounts for up to 60% of proteins present in the blood, transporting many endogenous biomolecules. It comprises of 3 domains (I,II,II), each with 2 subdomains (A,B); Sudlow I site (IIA) and Sudlow II site (IIIA) are important drug binding sites[1]. Drugs, which are chemicals used to treat diseases and illnesses or relieve symptoms when present in the blood, can bind to Human Serum Albumin (HSA)[2]. The extent to which the drug binds to HSA depends on the compound's chemical properties. Plants have been an important part of human diets since ancient ages. When plants are digested, phytochemicals, chemical compounds in plants, are metabolized and absorbed into the human body. Some of the bioactive molecules in plants were proven to possess some antioxidant, anti-cancerous, and neuroprotective effects, improving wellness overall[3]. The goal of this research is to explore the interaction between HSA and phytochemicals and check the presence of binding and binding sites using spectroscopic techniques.

Hypothesis

- ❑ Chosen phytochemicals do not have detrimental effects on HSA.

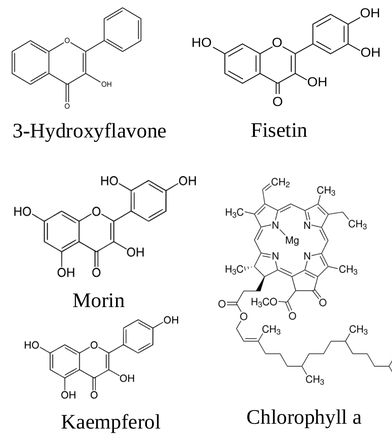
Objectives

- ❑ Analyze the changes in fluorescence properties of Tryptophan 214 in HSA in the presence of phytochemicals and vice versa.
- ❑ Investigate computational prediction of binding sites and confirm the results with spectroscopy.

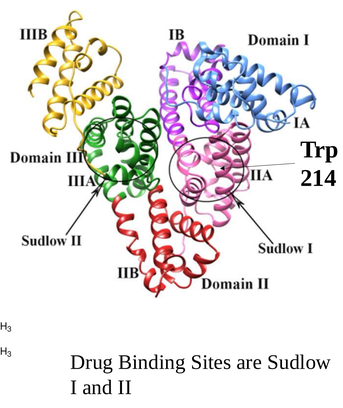
Methods and Materials

- ❑ **UV/Vis Absorption Spectroscopy:** Shimadzu UV 2550 spectrophotometer
- ❑ **Fluorescence Spectroscopy**: HORIBA Scientific FluoroMax Plus Fluorometer.
- ❑ **Docking**: AutoDock Vina[4,5] results are visualized with Pymol and BIOVIA Discovery Studio[6].

Representative Phytochemicals

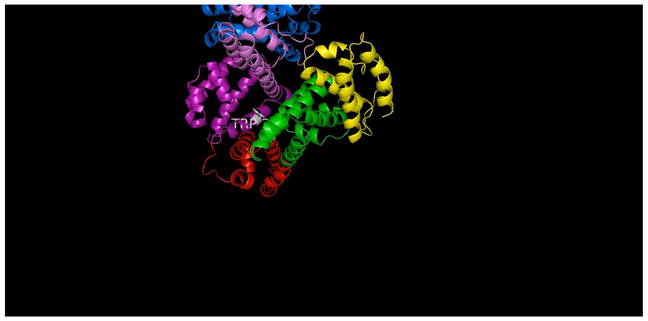


Human Serum Albumin

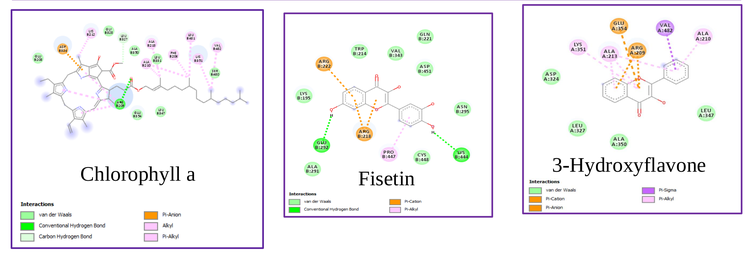


Drug Binding Sites are Sudlow I and II

Computational Docking

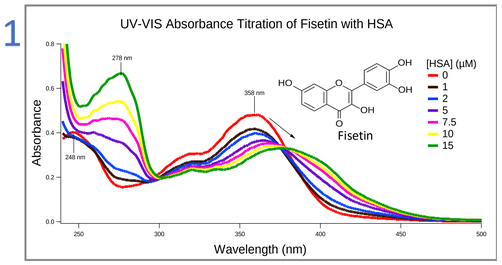


Interaction of Phytochemicals and Chlorophyll a with Surrounding Amino Acids in HSA



Binding Of Phytochemicals With HSA (Optical Spectroscopic Study)

1



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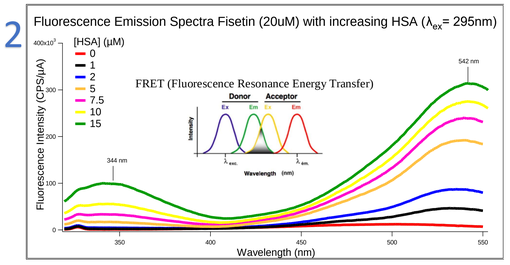

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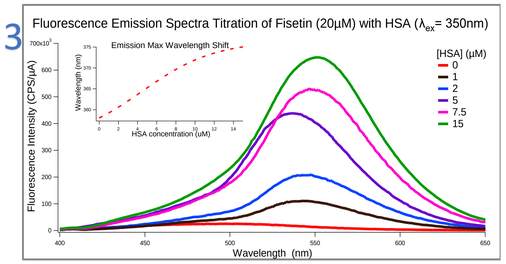

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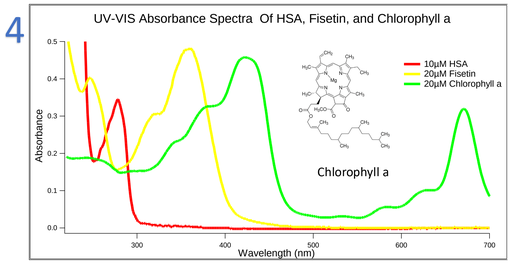

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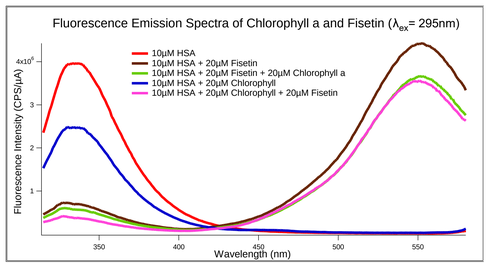

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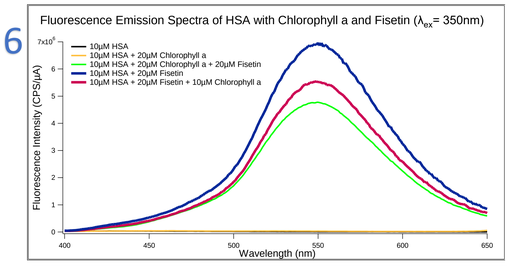

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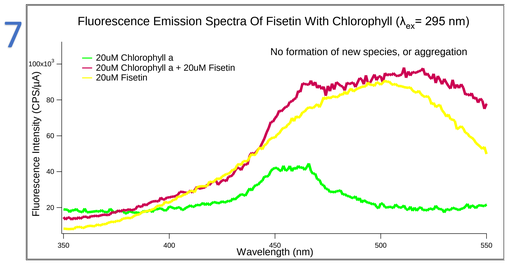

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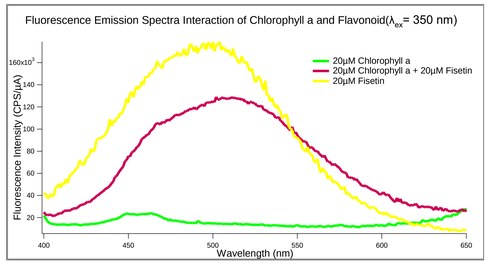

Observations: With increasing protein concentration, fisetin and chlorophyll bind with HSA. Fisetin and chlorophyll A both bind close to Tryptophan 214 residues, evidenced by the rise of FRET phenomena Chlorophyll displaces some fisetin which is dictated by the lowering of fluorescence intensity.

Conclusion

In this study, fisetin, 3-hydroxyflavone (3HF), morin, and chlorophyll a were confirmed to bind close to residue 214 of HSA in the Sudlow I site, due to the presence of Fluorescence Resonance Energy Transfer (FRET). These results agreed with docking results, with several conformations at the Sudlow I site, near Tryptophan 214. There was some competition between chlorophyll and flavonoid (3HF, morin, fisetin) at the mutual binding site.

Future Studies

- Investigate common phytochemicals' binding capacity to HSA.
- Study the displacement of phytochemicals with drugs known binding to HSA.

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