ASSIGNMENT: RESEARCH PAPER SUMMARY

Screening of Altered Metabolites and Metabolic Pathways in Celiac Disease Using NMR Spectroscopy

A class of medications known as nonsteroidal anti-inflammatory medicines (NSAIDs) is used to treat inflammation, fever, and pain. It is typically used to treat conditions that produce pain and inflammation, including arthritis, sprains, severe menstrual cramps, headaches, and sprains. Damaged tissue creates prostaglandins during an injury that are connected to the physiological processes of heat, pain, and inflammation. Cyclooxygenases (COX) enzymes, which catalyse the formation of prostaglandins and lower inflammation and pain, are inhibited by NSAIDs. COX comes in two varieties: COX-1 and COX-2. NSAIDs that simultaneously block COX-1 and COX-2 frequently result in digestive issues such ulcers in the esophagus, stomach, or small intestine.

One of the methods used in computer-aided drug design is molecular docking. By figuring out the ligand's ideal position inside the receptor, making it is possible to maximise the ligand-receptor interaction. Prediction of the binding can be made using the preferred ligand-receptor orientation.

In order to better understand how the ligand ipalbidine binds to the seven human COX-2 protein structures that are currently known, this work aims to change the ligand in order to increase its binding affinity. Due to Ipomea Alba's natural origin, this study will aid in the development of novel drugs that could potentially have less negative side effects than those now on the market. Because not every people or illness case responds well to a given treatment, the creation of an alternate medication is also crucial.

Modified ligands were successfully enclosed in the COX-2 protein structure and were able to bind to the binding site. It was found that by increasing the amount of hydrogen atoms on the ligand by converting the carbon double bond into a single bond, the binding affinity was reduced.

Ipalbidine with inverted chirality was the second modification. All binding affinities were higher for inverted chirality, suggesting increased effectiveness and bond strength. Clinical trials might be necessary to uncover potential adverse effects since a change in a drug's chirality could affect the drug's selectivity or overall effect. Initialization NSAIDs, often known as non-steroidal anti-inflammatory medicines, are a class of medications that reduce pain.

In order to compare the binding affinities of the modified ipalbidine, the unmodified ipalbidine (green line) served as a baseline. Focusing on the modification that resulted in a carbon double bond being replaced with a single bond to enable more hydrogen to form bonds with the ligand (blue line), the effects on the ligand's binding affinity are sporadic, with 5Fla, 5Fl9, and 5KIR experiencing a decrease in binding affinity while 5IKQ and 5IKT experience an increase.

The hydrophobicity of the inner surfaces of the binding site, which repels the ligand and lowers the binding affinity, may be the cause of this. For instances where changing the double bond to a single bond and so increasing the hydrogen atoms increases the binding affinity. Thus the evidence indicates that the inverted chirality has a higher binding affinity for ipalbidine, which suggests a more stable bond and greater spontaneity for the bond to form. a gentle reminder that the chirality of the nitrogen atom is the single factor that remains constant when chirality changes.

By changing the chirality of the oxygen atom and the carbon ring null throughout the docking process, the ligand's flexibility will rotate the ligand to improve the binding affinity.
The chirality and carbon double bond of the ligand ipalbidine were changed using the Avogadro software in order to enhance the quantity of hydrogen attached to the ligand. The modified ligands were able to bind to the same sites as unmodified ipalbidine and were successfully docked into seven COX-2 protein structures. According to the determined binding affinities, a weaker link was produced when the double bond was converted to a single bond, which increased the number of hydrogen atoms on the ligand. The hydrophobic lining of the Cox-2 binding site may have resulted in a weaker binding as a result of the added hydrogen atoms. in order to change the chirality. The nitrogen atom's chirality was reversed, which demonstrated more negative binding affinities across the board. This means better efficacy and bond strength. However, the change in the chirality of a drug may change the selectivity or effect of the drug as a whole, and therefore clinical trials may be required to see possible side-effects that may arise.