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MOLECULAR DOCKING ANALYSIS OF SELECTED CELOSIA ARGENTEA CONSTITUENTS AS HUMAN TRANSFFERINMODULATOR

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Abstract:
The phytoconstituents of *Celosia argentea* has been reported to posses various biological properties. This promoted us to carry out the docking study on the 20 ligands namely CelogentineE,CelogentinH,Palmitoleic acid, Octadecanoic acid Luteolin70glucoside,CelosinF,Linoleicacid,CelosinG,Hexadecanoic acid,celosinE,CelogentinK,CelogentinJ,CelogentinG,CelogentinC,CelogentinB,CelogentinF,Arachidonic acid,CelogentinD,CelogenamideA and Arachidic acid of the plant celosia argentea with the serum protein.These ligands were evaluated on the docking behavior of human transfferin protein (1A8F) using patch Dock online software.Docking and binding free energy analysis revealed that the ligand CelogentinD exhibited maximum binding energy towards human transfferin protein.The present study has paved a new insight in understanding the constituents of celosia argentea as potential iron contentor and can be used in therapeutics for iron deficiency anaemia.The leaves of the plants were dried for about a month without sunlight.A sample of single dried leaf from each plant was given to analyse the peaks of absorbance by Fourier transform Infrared Spectroscopy (FTIR) to denote the presence of metals.
Keywords: Transfferin protein,iron deficiency,ligands,Docking,Serum protein receptor,Celosia argentea,drug designing,CelogentinD.

1. Introduction

Iron deficiency is estimated to affect about one fifth of the world's population, and women and children are among the most severely affected. Evidence is mounting that iron deficiency anemia adversely affects brain development with measurable effects on children's behavior with learning disability,reduced work productivity,morbidity,mortality, motor development and cognition (Fikiru Dasa et al,.2018). In Chennai district of the state Tamil Nadu, south-India,50% of school age children (5-6years) and 37.46% of children(0-20 years) are anemic (Serena Josephine M et al.,2019). Iron bioavailability calculated using algorithms in regional diets ranged from 3.2 to 4.6 percent. Celosia argentea is one of unutilised plant. It is a high potential plant with 13.5 mg/100g of iron and known as a nutritious and healthy legume (Oluwafunmilayo Dorcas Adegbaju et al,2019). Ascorbic acid is a potent enhancer of iron absorption in humans which can counteract the inhibitory effect of phytic acid and polyphenols (Fikiru Dasa et al.,2018). Guava is a popular and easily available fruit for this community having 3111.67mg/10g of ascorbic acid (Ojukwu UP et al,2017).

1.1. Conventional iron proportion in human body

Iron is arranged as the twenty sixth element in the periodic table and is composed of the molecular weight of about 55.85.Iron is available in abundance in the earth but in trace amount within the human body.The below table is reffered for its fractions in milligram.(-Fikiru Dasa et al.,2018).

Table.1.1.Iron Proportion

Discrete factor	Iron Portion (mg)
Infants	250
Adult female	2000-3000
Adult male	3000-4000

1.2.Distribution of iron content in different establishments in the body

(-Fikiru Dasa et al.,2018).

Table.1.2.Iron establishment.

S.No.	Disposition	Percentage conformation
1.	Haemoglobin	60
2.	Myoglobin	5
3.	Heme and non-heme enzymes	5
4.	Ferritin	20
5.	Hemisederin	10

The iron has a major key function in the energy metabolism and in physiochemical processes.In the biological mechanisms such as the citric acid cycle , it exists in the enzyme aconitase,NADH dehydrogenase and succinate dehydrogenase by forming a linkage with sulphur in the mitochondria and cytosol of the cell for the energy production (sugar-breakdown) by ATP synthesis.Hence it is the bit-part of all the cells in the human body.Iron is entangled in the oxidation and reduction reaction by accepting and donating electrons.The physiochemical role of iron denotes its distribution of oxygen to the various hunks of the body through haemoglobin.Fe prevents Hydrogen peroxide accumulation alongside breaking the bond between hydrogen and oxygen.

1.3. Mechanism of Iron absorption

(-Richard et al.,1998) When a cuisine containing iron content is consumed,the iron is digested and absorbed by the duodenum and proximal jejunum within the small intestine.The heme and non-heme iron is engrossed by the process of endocytosis.Ferritin is preoccupied by transfferin receptor.

Iron deficiency anaemia predominantly occurs due to the reduced intake of iron,slight absorption and blood loss (because blood contains red-blood cells with iron containing haemoglobin).

In the early stage of anaemia,the serum iron concentration in transfferin protein is standrard at a normal condition.If left unnoticed,it gradually decreases followed by moderate decrease in the heam iron as the next pace leading to the severe stage of anaemia.The symptoms include impaired physical activity,reduced mood,reduced cognitive function,poor pregnancy related outcomes, weakness, fatigue, dyspnea, palpitations,sensitivity to cold,abnormalities in oral cavity and gastrointestinal tract and reduced capacity in work.The adolescent women are more susceptible to the disease.The infants,children,teenagers,women of child bearing (mensuration and chid bearing in fertile women) are the most commonly affected .

Excessive consumption of iron content results in iron overload in which iron floats without binding to serum protein.It causes bacterial infection and cardiomyopathy.It consequences in inadequeate synthesis of iron-binding protein.On the other hand if the iron absorption is regulated in a controlled manner, its excretion is unconstrained.This problem can be limited by appropriate diet and biological system.

1.4. Elucidation of the substances inhibiting iron absorption

(-Fikiru Dasa et all.,2018)

Table.1.3.Iron absorption inhibiting components

S.No.	Inhibiting module
1.	Presence of anti-nutrients such as phytates and tannin) in cereal based food products.
2.	Iron-binding phenolic compounds in tea,coffee,red wine.
3.	Some leafy vegetables,herbs,nuts and legumes.
4.	Calcium
5.	Soy protein

It is reported that 165mg of calcium inhibits fifty to sixty percentage of heme and non-heme iron absorption.The maximum diffidence occurs at the time when 300mg of calcium is specified in consumption.The intensity of inhibition remains stable at the lattar level (300milligram).The duration for the exposure of inhibition pertains about two hours.1000mg of Ca in twelve weeks showed no harmful effects.

Iron absorption is equal to nought when the iron containing edible product such as bran-bread comprises of high-phytate content.20mg of polyphenols present in black tea produces sixty six percentage of diffidence.Leaves of lead tree in Thailand known as Yog kratin make ninty percent inhibition.The plant species spinach and aubergin are gregarious inhibitors of iron absorption.Thirty six percentage of inhibition in iron absorption takes place when tea is consumed along with milk.Meanwhile twenty percentage of iron absorption is restricted when tea is exclusively utilized.Coffee inhibits ten percent of iron absorption due to the presence of chlorogenic acid.(-Richard et al.,1998).

1.5. Elucidations of the enhancers of iron absorption

(-Fikiru Dasa et all.,2018)

Table.1.4.Iron absorption supplements

S.No.	Enhancement module
1.	Ascorbic acid
2.	Meat ,fish and seafood

3.	Organic acids such as tartaric acid, citric acid, malic acid, lactic acid.

Ascorbic acid is potent enough as to enhance non-heme-iron absorption of about twenty five percent when consumed in the ratio of 2:1 along with the standard meal.Meat is the only exceptional supplement for heme iron absorption because of gastric acidic effects and chelation.Alcohol is another module for the increament of serum transfferin iron, ferritin , hence the chronic alcohol abusers have calculatedly higher ferritin concentrations compared to the non-drinkers.

Table.1.5.Provenance of iron in fruits and vegetables

(-Bhuvaneswari.S et al.,2015)

S.no.	Source	Mean Iron content (mg/100g)
1.	Apple	0.92
2.	Fig	1.32
3.	Ground nut	1.27
4.	Soya bean	1.65
5.	Dates	0.52
6.	Fenugreek leaves	2.40
7.	Spinach	0.58
8.	Raisins	0.88

Since the ascorbic acid enhances iron absorption the content of it is esteemed in the below table.

Table.1.6.Provenance of Ascorbic acid in fruits and vegetables

(-Bhuvaneshwari .S.,et al,2015)

S.No.	Source	Ascorbic acid content(mg/100g)
1.	Apple	14.97
2.	Fig	10.53
3.	Ground nut	5.44
4.	Soya bean	3.29
5.	Dates	1.99
6.	Fenugreek leaves	3.81
7.	Spinach	13.46
8.	Raisins	4.71

1.6.Iron Fortifications as a part of Iron sustenance

(-Ricardo Uauy et al.,2002)

Fortification is the worldwide methodology used for the lack of bioavailability of iron in foods to combat iron deficiency but the impact of it is not much documented.There are many practical and technical barriers arising in the production of fortified iron products.The staple foods like wheat,maize and rice are fortified with iron.Ferrous sulfate and fumarate are predominantly utilized.Fortifications have a wide range limitations due to which therapeutics for iron deficiency is promoted.

1.7.Iron Induction assay

(-Sarkar et al.,2007)

It is estimated that the herbal preparations prescribed in Ayurveda familiarly known as “Punarnava Mandura” for anaemic patients contains iron proportions (known as Mandura in Sanskrit) is composed of certain herbs listed in the table below.Hematinic evaluation of mandura (iron particals) on Mercury Chloride significantly increased the haemoglobin level in the anaemic rats.

Table.1.7.Illustrations of iron induction scrutiny

(-Swarnim Gupta et al.,2013)

S.no.	Ministrations	Serum iron induction(ng/mg cell protein)
1.	Saline control	17
2.	$FeCl_3$ and Ascorbic acid	1119
3.	B.diffusa (Punarnava leaves)	14
4.	T.ammi(Ommum seeds)	14
5.	A.paniculatus (Amaranth seeds)	20

6.	L.sativum (Garden cress seeds)	13
7.	M.sativa (Alfa alfa seeds)	15
8.	S.indicum(Tila seeds)	18
9.	A.racemosus(Asparagus roots)	17
10.	P.Longum (Pipli fruits)	15

1.8.Nutritional configuration in the iron-potent plant –Celosia argentea

(-Oluwafunmilayo Dorcas Adegbaju et al,2019).

Table.1.8.Nutriment conformation

S.No	Nutrient	Percentage composition (%)
1.	Carbohydrate	45.50
2.	Protein	5.17
3.	Fibre	3.53
4.	Fat	1.10
5.	Ash	22.43
6.	Dry matter	15
7.	Moister	8.84

The consignment of energy in Kilo-calorie per 100g is 234.45.It is reported that 800g of the plant contains 280g of sugar molecule,43g of amino acid content,35.7 g of fibrous mass,16.65g of lipid content,178.4g of residue,163g of dry matter and 80g of water content.(-Gloria aderonke otunola et al.,2019)

1.9.Mineral configuration in iron-potent plant-Celosia argentea

-(Oluwafunmilayo Dorcas Adegbaju et al,2019).

Table.1.9.Conformation of inorganic constituents

S.No.	Element	Constitution (mg/100g)
1.	Calcium	178.08
2.	Iron	15.25
3.	Magnesium	39.64
4.	Manganese	1.73
5.	Potassium	128.33
6.	Sodium	71.32
7.	Zinc	7.25
8.	Copper	3.75
9.	Phosphorous	38.01

The estimation illustrates that 100g of the plant contains 0.176% of manganese,0.375% of copper, 0.82% of zinc,2.74% of iron,5.33% of phosphorous,5.54% of magnesium,10.5% of sodium,27.9% of potassium and 29.1% of calcium.(-Antony Jide afolayan .,et al,2013)

1.10.Vitamin configuration in iron-potent plant-*Celosia argentea*

-(Oluwafunmilayo Dorcas Adegbaju et al,2019).

Table.1.10.Fibre constituents.

S.no.	Vitamin	Constitution (mg/100g)
1.	Retinol	48.20
2.	Thiamin	0.09
3.	Ascorbic acid	59
4.	Tocopherol	28.3

The data describes the presence of 0.0001% of Vitamin B ,with 0.028% of vitaminE ,0.058% 0f vitamin C and 0.046% of vitamin A proportions.

1.11.Essential amino acid configuration in the iron-potent plant-Celosia argentea.

-(Oluwafunmilayo Dorcas Adegbaju et al,2019).

Table.1.11.Micro peptide constituents.

S.No	Amino acid denotion	Constituent (g/100g)
1.	Arginine	4.85
2.	Valine	4.37
3.	Histidine	2.25
4.	Leucin	6.31
5.	Isoleucin	3.30
6.	Lysine	4.68
7.	Methionine	1.52
8.	Phenylalanine	3.94
9.	Threonine	3.47

The availability of peptide denotes that the plant contributes towards genetic manifestations in the body

1.12.Taxonomic Framework of *Celosia argentea*

-(Oluwafunmilayo Dorcas Adegbaju et al,2019).

Table.1.12.Codific Classification.

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Order	Caryophyllales
Family	Amaranthaceae
Genus	Celosia
Species	argentea
Binomial name	Celosia argentea

Celosia argentea is a vast range of flora with vascular system to conduct water and nourishments with two cotyledon which is edible.It is a flowering variety used in ornamentation of Amaranthacea family.

1.13.Human transfferin Protein

The human transfferin protein (HTf) is a protein which is present in the blood-plasma of humans . HTf is mainly secreted by the liver and is translated by the TFgene at a size of 76KDa.It is also synthesized by other tissues and organs such as the brain(choroid plexus and ventricular system). It is also present in some of the vertebrates other than humans and in some invertebrates.In humans,transfferin consist of a polypeptide chain of 679 aminoacids and two carbohydrate chains.The structure of HTf includes alpha helices and beta sheets forming two domains.It is a glycoprotein and its main function is the iron-binding mechanism that controls the level of free Fe in the biological fluids i.e.iron homeostatis in maintaining iron concentration.Transfferin has two highly specific (FeIII) affinity binding site in between the two globular lobes of N and C terminal sequences. The optimum p^H for the binding is 7.4. The molecular weight of the human transfferin protein is 80KDa. HTf also plays an importantant role in the production of red blood cells called erythropoiesis and in the areas of active cell division.Transfferin has a iron-bound receptor which is a homodimer linked to a disulphide bond.There are two types of transfferin receptors-TfR1 and TfR2.The TfR1 is bound to human transfferin and the TfR2 is bound to bovine transfferin.The transfferin level is inversely proportional to the inflammation in the surface of the tissue.The quantity of the human transfferin is referred to be ranged from 204 to 360 mg/dL.As an abnormal condition the transfferin level increases for patients with iron-deficiences,during pregnancies and for the individuals consuming oral contraceptives.The decrease in transfferin level leads to a genetic disorder known as atransfferinemia causing complications in heart,liver and in organs.HTf is a anti-cancer protein.HTf has an application in nanotechnology as it can be moved across the blood-brain barrier through the receptor-mediated brain capillaries endothelial cells for the treatment of the diseases like Alzeimer's and Parkinson's by making the nanoparticals the drug carriers bound to transfferin glycoprotein.These tranfferin conjugated nanopartical serves as a non-invasive drug for the therapeutic activity in the Cental nervous system related diseases.

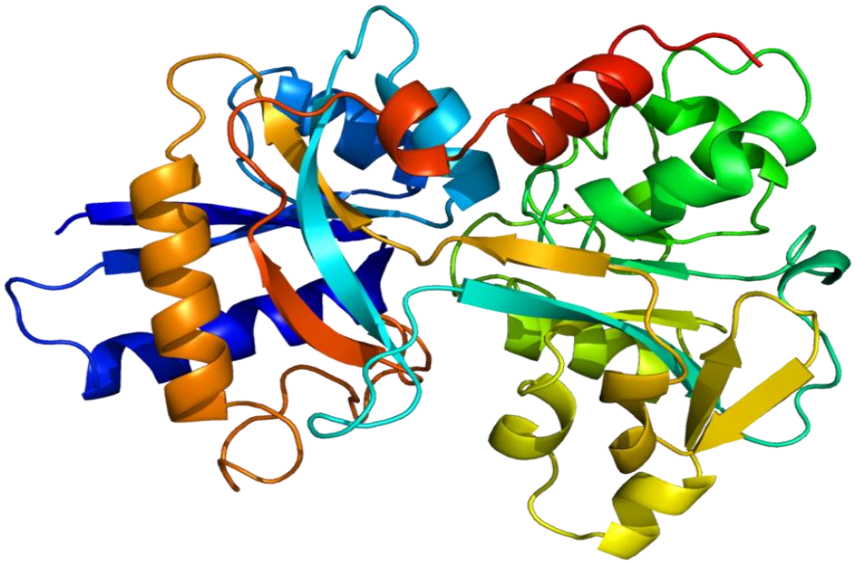


Figure.1.Structure of Transfferin protein.

2.Aim and objective

AIM :

To anticipate the treatment for iron-deficiency –Anaemia

OBJECTIVE:

- It is terminated by the Virtual screening process
- The physical properties are determined by the database of molinspiration,Swiss ADME
- The online software Patch Dock is accessed with 4.0 RMSD value.

3. Review of Literature:

(-Dorcus Adegbaju et al.,2019)

The common name of the plant Celosia argentea is Silver cock's comb.It is known as pannakerai in the South Indian language Tamil.It has wide range of applications and is used as a ancestral food.It is also used as a traditional medicine in the field of Ayurveda ,Siddha,Unani and Homeopathy.It is considered as a troublesome weed in some countries which reduces its significance.

Figure.2.Celosia argentea

Figure.3.*Celosia argentea* in Tamil Nadu

3.1.Botanical Description

It is an annual herb and is erect about 0.4 to 2 meters.Infloresence is dence and silvery.

3.2.Distribution

It is originally from tropical Africa ,but it has been spread early throughout Asia and Malayasia (-Smith et al.,1981).In India it is cultivated in Assam,Bihar,Gujarath,Karnataka,Maharashtra and Odisa.(-Pawan Kumar et al.,2011).

3.3.Applications of Celosia argentea

(-Sunil Kumar et al.,2011)

Celosia argentea is used as a colouring agent,preservative,flavor enhancer,maintains texture and body of the cuisine,serves as a sweetener and adds to the appearance of the food to which it is added.It replaces saffron (kunkuma poo in tamil) which is the colouring and flavouring module.It reduces the psychrophilic count and TBARS content in the food it is added.It is rated 7.10/8 in its overall acceptability.

3.4.Biological activities

3.4.1.Antidiabetic activity

Diabetes mellitus is a disease of metabolic disorder caused by the impairment of glucose usage associated with underlying factors for both hypoglycemia and hyperglycemia. Adequate consumption of green leafy vegetables reduces the risk of diabetes(-Harding et al.,101). Anti-diabetic activity of C. argentea root extracts on streptozotocin-Induced diabetic rats(Ghul et al.,102). The effect of extracts from C. argentea at 500mg/kg dose on diabetic rats after 2 weeks of treatment showed a significant decrease in glycaemic levels from 397.83 ±9.67 mg/dL to 99.33 ± 1.84 mg/dL, this translates to a reduction of 75%. The alcoholic extracts of Celosia argentea seeds have also been reported to reduce blood glucose in alloxan-induced diabetic rats after two weeks. A decrease of 27.8% and 38.8% in the blood glucose level was reported after 6 hours, at 250 and 500 mg/kg dose respectively . Both the aqueous and ethanolic fractions of C. argentea exhibited significant hypoglycemic activities on alloxan-induced diabetic rats after oral administration at 800 mg/kg dose.(-Shan et al.,104)

3.4.2.Anti-obesity potential

The low, crude fat content of the genus could be suitable in facilitating initial weight loss and subsequent weight stability. The impact of C. cristata extract on human adipogenesis CD34+/CD31− cells, using immunoselection/depletion approaches was evaluated(-Fituussi et al.,105). Results revealed that C. cristata extract reduces lipid content of progenitor cells undergoing adipogenic differentiation within 10 days at a dose of 0.5%; and a significant decrease in the expression of C/EBPα gene to a level of 56.0% was recorded. Hence the species could be explored for the treatment and management

3.4.3.Hepatoprotective activity

Liver health maintenance is one of the major therapeutic uses of Celosia species in traditional medicine . This has been supported by various modern scientific pharmacological findings .A three-day intragastric administration of celosin A and B (bioactive compounds from the species) at different doses of 1.0, 2.0 and 4.0 mg/kg had a modulatory effect on hepatic enzymes in 0.10% CCl4-induced liver damage in Kunming mice by lowering the levels of AST, ALT and ALP from 299 ±77, 167 ±26, 380 ±72 to 293 ±54, 162 ±42, 360 ± 75, respectively, at the highest dose of 4.0 mg/kg (-Xue et al.,106). Celosins from C. cristata decreased the level of lipid peroxidation in a carbon tetrachloride (CCl4)-induced hepatotoxic mice.

The levels of antioxidant enzymes (SOD, CAT and GSH-Px) were reported to increase significantly with an oral dose of 0.1, 0.2 and 0.4 mg/kg. Celosia cristata flower extracts protect against tert-butyl hydroperoxide-induced oxidative hepatotoxicity. In vitro, the extracts prevented reactive oxygen species (ROS) generation and

mitochondrial membrane depolarization in t-BHP-induced hepatotoxicity in Chang cells . Also, in vivo administration of Celosia cristata flower extracts (100 and 500 mg/kg body weight) orally to rats consecutively for five days before a single dose of t-BHP (2 mmol/kg, i.p.) significantly ($p < 0.05$) protected the liver cells by lowering serum levels of glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT) i.e. as well as decreased hepatic lipid peroxidation and serum triglyceride against t-BHP-induced oxidative stress.

3.4.4.Anti-Cancer activity

Celosia species are potent anti-tumor agents .It is reported that 28 µg/mL of methanolic extracts of C. argentea showed significant cytotoxic activity comparable to methotrexate, a standard anti-cancer drug(-Rub et al.,101); while it is also reported the anti-metastatic effect of C. cristata extracts on liver metastasis of murine colon 26-L5 carcinoma cells and that C. cristata exerted mitogenic activity of on the spleen cells at concentration of 1000 µg/mL (Hayakawa et al.,112). The anti-tumour activities of four triterpenoid saponins from Celosia on five human cancer cell lines at concentrations less than 100 µg/mL (Wu et al.,110). Inhibition of cancer cells at concentration range of 24–30 µg/mL was recorded for the entire cancer cells tested. The aerial parts of Celosia argentea extracted with 70% ethanol and water, reduced myelosuppression and enhanced immune response against-induced myelosuppression in Swiss mice(-Nirmal et al.,113). The effect of ethanolic extract of C. argentea on the viability of two cancer cell lines (SiHa and MCF-7) using MTT assay (-Rab et al.,110). The outcome of the study showed that C. argentea exhibited a potent anti-cancer activity against both cell lines at concentration of 28 µg/mL, but does not have any toxicity effect towards normal cells investigated. The plants from Celosia were consumed by prisoners of war in Thailand to prevent nutritionally related diseases and also as an anti- cancer agent (Navarra 114.,et al,114).

3.4.5.Antimicrobial and Anthelmintic potential

The extracts from Celosia species has been reported to show inhibitory activities against Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans and Aspergillus niger at concentrations ranging from as low as 3.125 to 50 µg/mL . The antimicrobial activities of C. cristata and reported that methanolic and ethanolic extracts of the species inhibited the growth of S. aureus, B. subtillus and C. albicans at 0.125, 0.5 and 1 mg/mL respectively (Yun et al.,116). The aqueous extract of C. cristata showed significant anthelmintic activity on adult worms of Pheretim posthuma at 100–200 mg/mL (-Rubini et al,.112).

3.4.6.Antinociceptive and Antiurolithiatic activities

A strong antinociceptive effect of the methanolic extract of C. cristata in

mice at a dose of 400 mg/kg, providing a rationale for its traditional use for the treatment of painful conditions (Islam et al.,118). The antiurolithiatic activity of ethanolic extract of C. argentea seeds in rats(-Joshi et al.,119).

The authors found that C. argentea seed extracts prevented the formation of kidney stones at doses of 250 and 500 mg/kg, thus preventing impairment of renal function. The extracts of C. argentea roots exhibited significant prophylactic effect on renal stone of ethylene glycol induced rats at both the standard drug used in the study.(-Kachichi et al.,117)

4. Materials and methods

4.1.Ligand preparation

Chemical structures of the 20 ligands namely 1)Celosin G(CID53236073) 2) Celosin E(CID53239472) 3)Celosin F(CID101788473) 4)Celogenamide A(CID11263281) 5)Arachidic Acid(CID10467) 6)Arachidonic Acid(CID 444899) 7)Linoleic Acid(CID5280450) 8)Palmitoleic Acid(CID445638) 9)Hexadecanoic Acid(CID985) 10) Octadecanoic Acid(CID5281) 11)Luteolin 7-O-Glucoside(CID45933934) 12)Celogentin H(CID101236343) 13)Celogentin B(CID20704435) 14)Celogentin C(CID10985937) 15)Celogentin D(CID76185975) 16)Celogentin E(CID 101236340) 17)Celogentin F(CID101236341) 18)Celogentin G(CID101236342) 19)Celogentin J(CID101236344) 20)Celogentin K(CID101344858) were retrieved from Pubmed compound database.(www.pubmed.com)

4.2.Target Protein Identification and Preparation

The three-dimensional structures of the HTf (PDB ID: 1A8F with resolution of 1.8 Å) was obtained from the Research Collaborator for Structural Bioinformatics (RCSB) Protein Data Bank (www.rcsb.org). The protein was pre-processed separately by deleting other chains (A, B, and C) and the ligands(Fe,CO_3), as well as the crystallographically observed water molecules (water without hydrogen bonds).

4.3.Molecular Descriptors Calculation

Molinspiration online database was used to calculate 13 descriptors (www.molinspiration.com); logP, polar surface area, molecular weight, number of atoms, number of O or N, number of OH or NH, number of rotatable bonds, volume, drug likeness including G protein coupled receptors (GPCR) ligand, ion channel modulator, kinase inhibitor, and nuclear receptor ligand, and number of violations to Lipinski's rule, for all selected 20 ligands.

4.4.Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET)

The ADMET test was performed using Discovery Studio® 3.1 (Accelrys, San Diego, USA). ADMET analysis was performed using human intestinal absorption (HIA), aqueous solubility (AS), blood brain barrier (BBB), cytochrome P450 2D6 (CYP2D6), plasma protein binding (PPB), and hepatotoxicity (HT) descriptors.

4.5.Docking studies

Docking studies were carried out by the crystal structure of Human serum transfferin retrieved from protein data bank using patch dock.

5. Results and discussion

The 2D structure of the 20 ligands retrieved are listed in the below table.

Table.5.1.Pubmed data

s.no	Compound name	Compound CID	Canonical SMILES
1.	Celosin G	53236073	CC1C(C(C(C(O1)OC(=O)C23CCC(CC2C4=CCC5C6(CCC(C(C6CCC5(C4(CC3)C)C)(C)C(=O)O)OC7C(C(C(C(O7)CO)O)O)O)C)(C)C)OC8C(C(C(C(O8)C)OC9C(C(C(O9)C(=O)O)O)O)O)O)O)O)O
2	Celosin E	53239472	CC1(CCC2(CCC3(C(=CCC4C3(CCC5C4(CC(C(C5(C)C(=O)O)OC6C(C(C(C(O6)C(=O)O)O)O)O)O)C)C(=O)OC2C1)C)C)C
3	Celosin F	101788473	CC1C2C3=CCC4C5(CC(C(C(C5CCC4(C3(CCC2(CCC1=C)C(=O)O)C)C(=O)O)(C)C(=O)O)OC6C(C(C(CO6)O)O)O)O)C
4	Celogenamide A	11263281	CC(C)C1C(=O)NC(C(=O)NC(C(=O)NC(CC2=CN(C(C(=O)N1)NC(=O)C(CC3=CC=C(C=C3)O)NC(=O)C4CCCN4C(=O)C5CCC(=O)N5)C6=CC=CC=C26)C(=O)NC(CCCCN)C(=O)O)CO)CC7=CC=CC=C7
5	Arachidic Acid	10467	CCCCCCCCCCCCCCCCCCCC(=O)O
6	Arachidonic Acid	444899	CCCCCC=CCC=CCC=CCC=CCCCC(=O)O
7	Linoleic Acid	5280450	CCCCCC=CCC=CCCCCCCCC(=O)O
8	Palmitoleic Acid	445638	CCCCCCC=CCCCCCCCC(=O)O
9	Hexadecanoic Acid	985	CCCCCCCCCCCCCCCC(=O)O
10	Octadecanoic Acid	5281	CCCCCCCCCCCCCCCCCC(=O)O
11.	Luteolin 7-O-Glucoside	45933934	C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)OC4C(C(C(C(O4)CO)O)O)O)O)O)O
12.	Celogentin H	101236343	CCC(C)C1C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(=O)NC(C(=O)N1)CC(C)C)NC(=O)C(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)CNC(=O)C(C2=O)CCCN=C(N)N)C(=O)NC(CC(=O)O)C(=O)O)N=C6
13.	Celogentin B	20704435	CC(C)CC1C(=O)NC(C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)N1)NC(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)C(NC2=O)CCCN=C(N)N)C(=O)NC(CC7=CN=CN7)C(=O)O)N=C6)C(C)C

14.	Celogentin C	10985937	CC(C)CC1C(=O)NC(C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)N1)NC(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)C(NC(=O)C7CCCN7C2=O)CCCN=C(N)N)C(=O)O)N=C6)C(C)C
15.	Celogentin D	76185975	CC(C)CC1C(=O)NC(C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)N1)NC(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)C(NC2=O)CCCN=C(N)N)C(=O)NC(CC7=CN=CN7)C(=O)NC(CCCCN)C(=O)O)N=C6)C(C)C
16.	Celogentin E	101236340	CC(C)CC1C(=O)NC(C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)N1)NC(=O)C(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)CNC(=O)C(C2=O)CCCN=C(N)N)C(=O)NC(CC(=O)O)C(=O)O)N=C6)C(C)C
17.	Celogentin F	101236341	CC(C)CC1C(=O)NC(C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)N1)NC(=O)C(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)CNC(=O)C(C2=O)CCCN=C(N)N)C(=O)NC(CCCN=C(N)N)C(=O)O)N=C6)C(C)C
18.	Celogentin G	101236342	CCC(C)C1C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)NC(C(=O)N1)CC(C)C)NC(=O)C(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)CNC(=O)C(C2=O)CCCN=C(N)N)C(=O)O)N=C6
19.	Celogentin J	101236344	CCC(C)C1C(=O)NC2CC3=C(NC4=C3C=CC(=C4)C(C(C(=O)NC(C(=O)N1)CC(C)C)NC(=O)C(=O)C5CCC(=O)N5)C(C)C)N6C=C(CC(NC(=O)CNC(=O)C(C2=O)CCCN=C(N)N)C(=O)NC(CCCN=C(N)N)C(=O)O)N=C6
20.	Celogentin K	101344858	CC(C)CC1NOC(C(C2=CC3=C(C=C2)C(CC(NOC(NO1)C(C)C)C(=O)NC(CCCN=C(N)N)C(=O)NCC(=O)NC(CC4=CN=CN4)C(=O)O)(C(=O)N3)O)C(C)C)NC(=O)C5CCC(=O)N5

5.1. Molecular Descriptors Analysis

Drug development is expensive and the most poorly behaved compounds toward physicochemical properties need to be weeded out early to prevent or minimize failure in pre-clinical stages/Phase I clinical trials. Thus, screening compounds based on Lipinski's rule of five is important which in the candidate drugs that comply with rule have been shown to have lower attrition during clinical trials. In the present study, all the 20 ligands selected from Celosia argentea composition showed no violation toward Lipinski's rule. The bioactivity score, was set to be (>0) active, (–5.0 to 0.0) moderate active, (<–5.0) inactive. However, for most descriptors these compounds exhibited active to moderate active scores with none showing inactive score (<–5.0) as shown in the below table.

Table.5.2.Physical properties of ligands

S.No.	Ligands	milogP	TPSA	natoms	MW	nON	nOHNH	Nviolations	nrotb	volume
1.	CelosinG	0.28	388.05	78	1117.24	24	13	3	12	995.73
2.	CelosinE	2.68	211.28	48	678.82	12	7	3	5	623.93
3.	CelosinF	1.83	211.28	47	662.77	12	7	3	5	602.03
4.	CelogenamideA	-.3.67	361.81	79	1092.22	24	13	3	18	980.70

5.	Archidic acid	8.73	37.30	22	312.54	2	1	1	18	358.63
6.	Archidonic acid	6.42	37.30	22	304.47	2	1	1	14	333.88
7.	Linoleic acid	6.86	37.30	20	280.45	2	1	1	14	312.65
8.	Palmitoleic acid	6.57	37.30	18	254.41	2	1	1	13	285.24
9.	Hexadecanoic acid	7.06	37.30	18	256.43	2	1	1	14	291.42
10.	Octadecanoic acid	8.07	37.30	20	284.48	2	1	1	16	325.03
11.	Luteolin70glucoside	0.19	190.28	32	448.38	11	7	2	4	364.19
12.	Celogentin H	-3.94	439.55	81	1129.24	28	15	3	17	1008.13
13.	Celogentin B	-3.15	396.79	77	1067.22	26	15	3	15	961.79
14.	CelogentinC	-2.54	359.32	74	1027.20	24	13	3	11	932.70
15.	CelogentinD	-4.19	451.91	86	1195.40	29	18	3	21	1088.50
16.	CelogentinE	-4.37	439.55	80	1115.22	28	15	3	16	991.33
17.	CelogentinF	-4.52	466.66	83	1156.32	29	18	3	18	1043.77
18.	CelogentinG	-2.55	373.15	73	1014.15	24	13	3	13	916.11
19.	CelogentinJ	-4.17	466.66	84	1170.34	29	18	3	19	1060.57
20.	CelogentinK	-2.59	388.99	70	985.11	26	16	3	19	889.28

5.2. ADMET Analysis

The ADMET (Absorption,Distribution,Metabolism,Excreation and Toxicity) profile of 20 ligands is listed in the table below.

Table.5.3.ADMET figures

S.no.	Ligand	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	LogKp(skin permeation)
1.	Celosin G	Low	No	Yes	No	No	No	No	No	-12.51cm/s
2.	Celosin E	Low	No	Yes	No	No	No	No	No	-7.57cm/s
3.	Celosin F	Low	No	No	No	No	No	No	No	-9.46cm/s
4.	CelogenamideA	Low	No	Yes	No	No	No	No	No	-13.27cm/s
5.	Arachidic acid	Low	No	No	Yes	No	No	No	No	-1.61cm/s
6.	Arachidonic acid	High	No	No	Yes	No	Yes	No	No	-3.20cm/s
7.	Linoleic acid	High	Yes	No	Yes	No	Yes	No	No	-3.05cm/s
8.	Palmitoleic acid	High	Yes	No	Yes	No	Yes	No	No	-3.18cm/s
9.	Hexadecanoic acid	High	Yes	No	Yes	No	Yes	No	No	-2.77cm/s
10.	Octadecanoic acid	High	No	No	Yes	No	No	No	No	-2.19cm/s
11.	Luteolin7-0-glucoside	Low	No	Yes	No	No	No	No	No	-8.00cm/s
12.	CelogentinH	Low	No	Yes	No	No	No	No	No	-13.07cm/s
13.	CelogentinB	Low	No	Yes	No	No	No	No	No	-12.60cm/s
14.	CelogentinC	Low	No	Yes	No	No	No	No	No	-11.98cm/s
15.	CelogentinD	Low	No	Yes	No	No	No	No	No	-15.13cm/s
16.	CelogentinE	Low	No	Yes	No	No	No	No	No	-13.24cm/s
17.	CelogentinF	Low	No	Yes	No	No	No	No	No	-13.96cm/s
O	CelogentinG	Low	No	Yes	No	No	No	No	No	-11.58cm/s
19.	CelogentinJ	Low	No	Yes	No	No	No	No	No	-13.56cm/s
20.	CelogentinK	Low	No	Yes	No	No	No	No	No	-14.13cm/s

Table.5.4.Bioactivity profile

S.no	Ligand	GPCR ligand	Ion channel	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1.	CelosinG	-3.75	-3.85	-3.88	-3.80	-3.69	-3.71
2.	CelosinE	-0.24	-1.08	-1.00	-0.33	0.00	-0.18
3.	CelosinF	-0.14	-0.89	-0.87	-0.19	0.10	0.05
4.	CelogenamideA	-3.71	-3.83	-3.84	-3.86	-3.61	-3.77
5.	Arachidic acid	0.16	0.05	-0.13	0.23	0.14	0.18
6.	Arachidonic acid	0.32	0.16	-0.09	0.35	0.19	0.35
7.	Linoleic acid	0.29	0.17	-0.16	0.31	0.12	0.38
8.	Palmitoleic acid	0.08	0.08	-0.35	0.14	-0.04	0.26
9.	Hexadecanoic acid	0.02	0.06	-0.33	0.08	-0.04	0.18
10.	Octadecanoic acid	0.11	0.05	-0.20	0.17	0.06	0.20
11.	Luteolin7-0-glucoside	0.09	-0.02	0.15	0.27	-0.01	0.42
12.	CelogentinH	-3.71	-3.82	-3.88	-3.91	-3.56	-3.76
13.	CelogentinB	-3.63	-3.75	-3.80	-3.88	-3.52	-3.72
14.	CelogentinC	-3.54	-3.71	-3.76	-3.82	-3.21	-3.67
15.	CelogentinD	-3.77	-3.85	-3.89	-3.95	-3.71	-3.83
16.	CelogentinE	-3.69	-3.81	-3.86	-3.90	-3.54	-3.75
17.	CelogentinF	-3.75	-3.85	-3.89	-3.92	-3.62	-3.79
18.	CelogentinG	-3.54	-3.72	-3.78	-3.78	-3.04	-3.63
19.	CelogentinJ	-3.76	-3.85	-3.90	-3.90	-3.64	-3.80
20.	CelogentinK	-3.47	-3.74	-3.76	-3.81	-3.81	-3.64

5.3.Docking studies with HTf

The Docking survey includes the compound CelogentinD had the maximum interactions whereas the compounds CelogentinE,Palmitoleic acid,octadecanoic acid,hexadecanoic acid etc had no interaction,the rest had medium level of iron-binding at the amino acid site lysine,Threonine,Serine,Tyrosine etc.

Table.5.5.Binding affinities

S.No	Compound name	ACE value	No. of interactions	Amino acid binding site	Wavelength(resolution)
1.	Celosin G	-322.1	one	Thr93	2.1
2.	Celosin E	-24.30	three	Tyr45 Arg50 Asn75	3.4 3.2 2.7
3.	Celosin F	-306.9	one	Tyr317	2.3
4.	CelogenamideA	-147.7	four	Tyr238 Tyr238 His300 Lys276	2.9 2.4 3.1 3.0
5.	Arachidic acid	-86.85	Nil	Nil	Nil
6.	Arachidonic acid	-227.6	three	Leu293 Arg124 Arg124	2.4 2.7 3.1
7.	Linoleic acid	-82.96	Nil	Nil	Nil

8.	Palmitoleic acid	-199.0	Nil	Nil	Nil
9.	Hexadecanoic acid	-199.4	Nil	Nil	Nil
10.	Octadecanoic acid	-92.22	Nil	Nil	Nil
11.	Luteolin70glucosi-de	-148.8	four	Thr181 Lys196 Ser189 Ser189	2.8 2.9 2.9 2.2
12.	Celogentin H	-154.0	three	Lys291 Lys291 Lys291	2.9 2.1 2.5
13.	Celogentin B	-196.2	three	Asn75 Arg50 Ala162	2.8 3.3 2.2
14.	Celogentin C	-415.4	two	Tyr136 Tyr136	3.1 2.6
15.	Celogentin D	-193.9	five	Trp128 Arg327 Arg327 Tyr45 Trp128	3.2 2.5 3.3 2.6 2.6
16.	Celogentine E	-324.3	Nil	Nil	Nil
17.	Celogentin F	-105.6	three	Tyr45 Tyr45 Tyr68	2.9 2.3 3.3
18.	Celogentin G	-194.31	three	Arg50 Ser44 Gly176	3.3 3.2 2.9
19.	Celogentin J	-267.7	two	Arg50 Asp163	2.9 3.2
20.	Celogentin K	-295.5	Nil	Nil	Nil

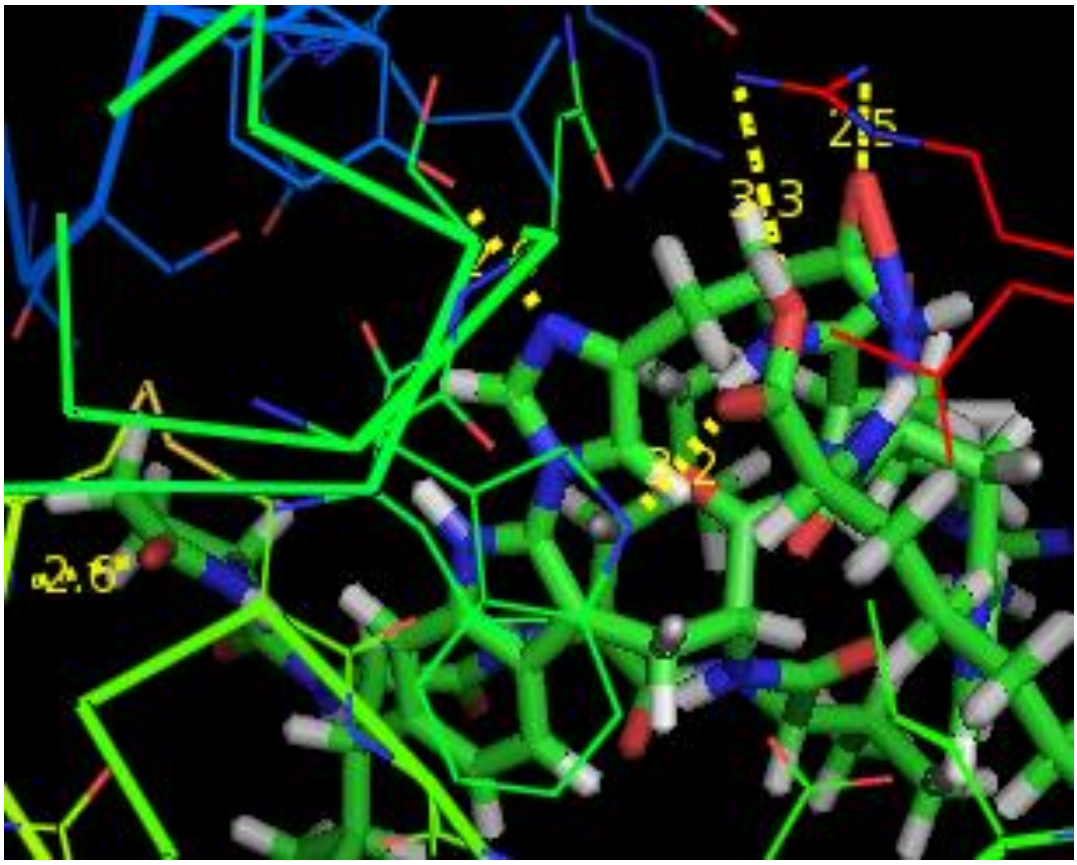


Figure.4. Celogentin D linkage with HTf

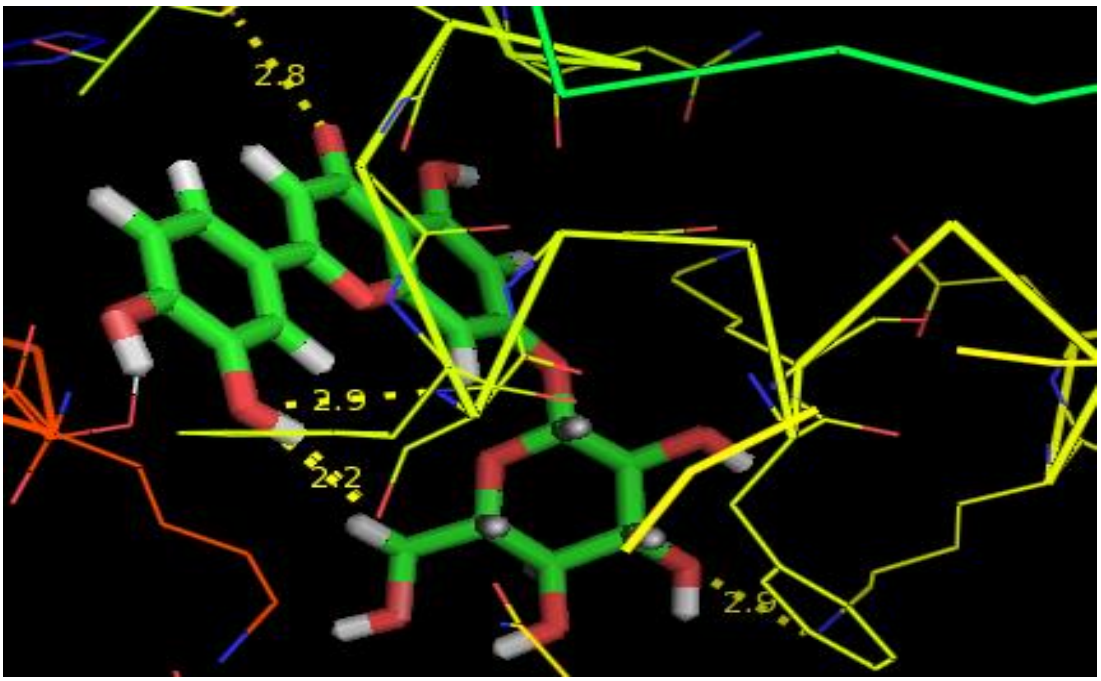


Figure.5.Luteolin7-0-glucoside linkage with HTf

Figure.6.CelogenamideA linkage with HTf

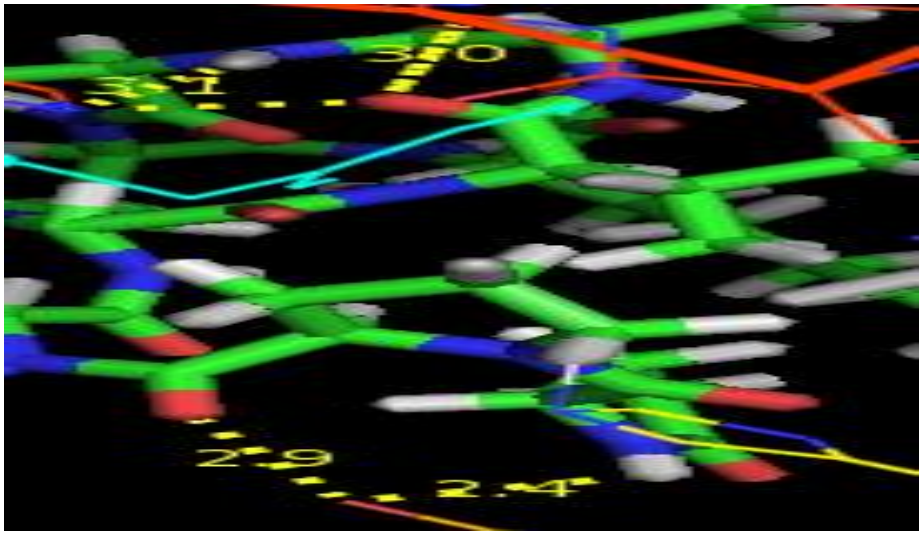
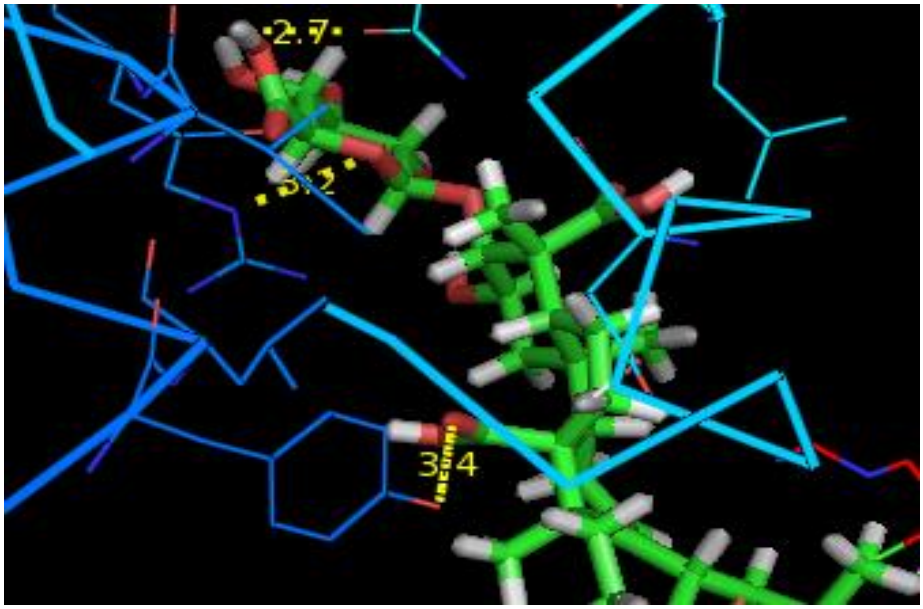


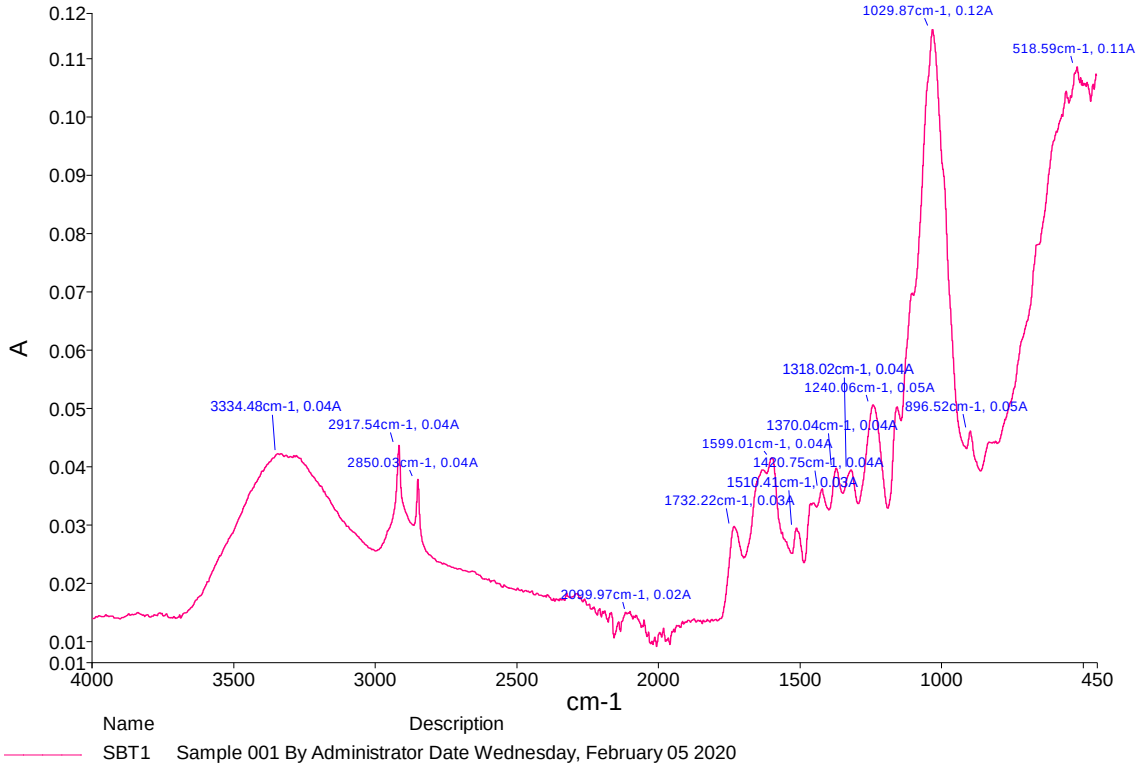
Figure.7.CelosinE linkage with HTf



5.4.FTIR Repercussion

The FTIR analysis indicated the presence of trace metals in Celosia argebtea which includes iron ,copper,zinc etc

Figure.8.FTIR output



6. Conclusions

In the present study,13 ligands out of 20 in Celosia argentea showed the potential to dock and bind with HTf(1A8F).Among the ligands only hexadecanoic acid,octadecanoic acid,CelogentinE,Palmitoeic acid ,Linoleic acid,CelogentinK and Arachidic acid failed to Dock with HTf.Hence it is strongly suggested that the results of this present study might provide a new insight in understanding these 20 ligands as potential acceptors in relation to the treatment of iron-deficiency disease.

7. Future Directions:

This insilico project can be further followed by invivo studies through the administration of the effective components to the laboratory animals and estimating the efficiency of the plant in curing anaemia.

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