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Morinda Coreia: An Overview for It's Pharmacological Activities & Docking Studies Of Rubiadin

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ABSTRACT:

Natural sources have been used as a medicine for curing diseases since early ages. Morinda coreia has been recognized as important herb for diagnosing various physiological disorders worldwide. It's also known as the Morinda tree or Indian mulberry. Morinda coreia is a flowering plant in the Rubiaceae family, which includes coffee. Which is having many medicinal uses such as diabetes, arthritis, liver diseases, cancer, gastric ulcer, diarrhea, dysentery, the plant can be utilized to treat hypertension, difficult period, joint pain, diabetes, gout, gum disease, sties, and Mental illness.On writing overview, the investigations shows that numerous exercises have been done on various parts including fruit, bark, leaves and flowers are used all alone for individual healthful and remedial qualities,such as anti-diabetic, anti-inflammatory, anti-microbial, anti-oxidant, anti-ulcer, wound healing, larvicidal, urolithiatic, anti-cancer. Different chemical constituent has been isolated such as iridiod glucosides, phenolic glycoside, secoiridoid glucoside and anthraquinone glycoside.Docking studies has been done on a particular chemical constituenti.eRubiadinwhich is also present in the plant Rubia cordifolia. Where Rubiadin which is majorly present in Morinda coreia.

KEYWORDS: Morinda coreia, Indian mulberry, Rubiadin, anti-diabetic, anti-inflammatory, anti-microbial, anti-oxidant, woundhealing, larvicidal, anti-cancer, docking studies,cancer targeted proteins, DHFR, α-amylase**.**

INTRODUCTION:

*Morinda coreia*belongs to the Rubiaceae family, is a traditional medicinal and colour delivering plant (synonyms; *Morinda pubescens*, *Morinda tinctoria*).India, Southeast Asia, and Polynesia are its normal living species[1].Traditionally, the whole plant number of ailments such asdiabetes, arthritis, liver diseases, cancer, gastric ulcer, diarrhea, dysentery, also used as an antiviral agent, anti-inflammatory agent, anti-convulsant, as astringent, anti-bacterial agent and alsoused in other heart disease[2].The plant is called by many names (Table no.1). In Telugu it is called as Maddi, in hindi as Aal, in Sanskrit as Paphanah, in Tamil as Mannanunai, Mannanatti, in kannada asHaladipavate, in Malayalam as Mannappavitta, in Urdu as Togarmughalai. As the names suggest the plant belongs to South India and is widely seen in the arid and semiarid regions of the plateau. In English it is called as Indian mulberry plant[3].

M. coreia is an ethno-therapeutic plant that includes metabolites such as anthraquinones, phenolics, aucubin, scopoletin, asperuloside, nutrients A and C, alkaloids, flavone glycosides, terpenoids, linoleic acid, saponins, tannins, and phenols[4]. Dyspepsia, gastropathy, loose stools,

sores, stomach ulcers, gout, sarcocele fever, aggravation, hernia, and other styptic, alexiteric, stomachrelated, carminative, febrifuge, and tonic are all treated with the herb[5,6].It revealed a broad antibacterial range[7],antibacterial[8],and antihypertensive activities[9].The plant can be utilized to treat hypertension, difficult period, joint pain, diabetes, gout, gum disease, sties, and Mental illness[10,11].It's also used to make the morindone dye known in India as "Suranji." Cotton, silk, and wool are dyed with morindone in crimson, chocolate, and purple tones. When the plant is three to four years old, the coloring matter is gathered mostly from the root bark. Morindin is the active ingredient isolated as a glucoside, which when hydrolyzed creates the colour[12].

The fresh fruits of *M. coreia* are high wealth in protein, starch, nutrient, and mineral substance, and can be utilized to supplant Noni (*Morinda citrifolia*) fruits.They have more ascorbic corrosive and niacin than Noni organic products, in spite of the fact that riboflavin and thiamine are more prominent in the dried fruit[13].*Morinda coreia* is a Southeast Asian tree also known as Yo-Paa in Thai. Conventional Thai (Isarn) medication utilizes its bark and wood to treat malarial fever.Eight iridiod glucosides, one phenolic glycoside, one secoiridoid glucoside, and one anthraquinone glycoside were found in the leaves and parts of *M. coreia*[14].Roots contain seven anthraquinones and one anthraquinone glycoside[15].

TAXONOMICAL CLASSIFICATION:

- **Kingdom:** Plantae
- **Phylum:** Tracheophytes
- **Class:** Angiosperms
- **Order:** Gentianales
- **Family:** Rubiaceae
- **Genus:** Morinda
- **Species:** coreia

SYNONYMS:

- *Morinda coreia*
- *Morinda pubescens*
- *Morinda tinctoria*
- *Morinda exserta*

COMMON NAMES

Sl.no	Languages	Common names
1.	English	Indian Mulberry, Morinda tree
2.	Hindi	Aal
3.	Tamil	Mannanunai, Mannanatti
4.	Malayalam	Mannappavitta
5.	Telugu	Maddi
6.	Kannada	Haladipavate, Maddi
7.	Urdu	Togarmughalai
8.	Sanskrit	Paphanah

TABLE NO.1 Common names in different languages

RANGE:

E. Asia - India, Sri Lanka, Thailand, Cambodia, Laos, Vietnam, Indonesia.

HABITAT:

Usually found in dry forest in India and Sri Lanka.

PROPERTIES:

Habit: Evergreen tree

Height: 8.00 m

Cultivation status: Cultivated, Wild

USES:

MEDICINAL USES:

The plant has been extensively used in Thai traditional medicine. In general, the centre of wild woods noni has been utilized to treat feminine problems, as a tonic for stomach and blood balance.Because of its terrible odour, the fruit is rarely utilised as a medicine. However, it was discovered that the beverage made by fermenting the fruits was capable of inhibiting enteropathogenic bacteria and included a high potassium content.

OTHER USES:

Linen and woollen items are dyed with a dye derived from the root bark.The root's bark is used

to colour red and yellow things. “Suranji” is the brand name for the Morindone dye extracted from the root bark. It's used to dye cotton, silk, and wool in crimson, chocolate, and purple hues.When the plants are three to four years old, the colouring matter is taken mostly from the root bark.To generate liquid manure, the fruit can be fermented with molasses.The attractive wood comes in a variety of colours, including red and yellow with red streaks.It's medium-hard, close-grained, and long-lasting. Plates and dishes are made of it[16].

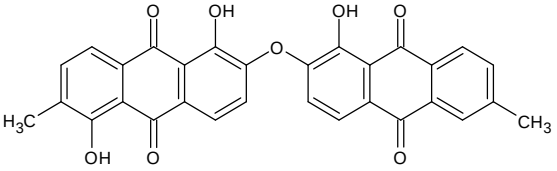
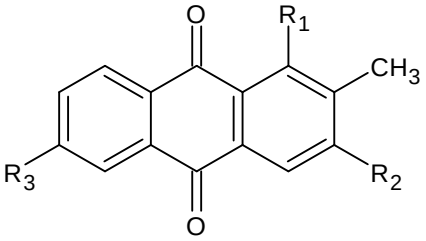
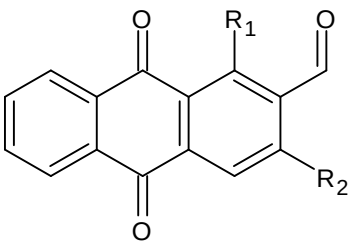
PLANT PROFILE:

The *Morinda coreia*(Fig no.1) is a tiny evergreen shrub or tree that grows at the height of 5-10 meters. The stem is crooked and short, with rough bark and extensive longitudinal incisions.Leaves are 15-25 cm long, oblong to lancelike, and oriented in opposite directions.Flowers are spherical heads that are 3-5 cm across and on a stem that is 2-3 cm long. There is one little linear leaf near the flower-head stem. The blooms are tubular, white, and perfumed, with a length of around 2 cm. The petals of the oblong flower are roughly 1 cm length and 3-7 in number. Stamens outnumber petals by a factor of ten.Green syncarps with a diameter of 2-2.5 cm. The plant is widely grown in India to produce the morindone dye known as "Suranji.Morindone is used to dye cotton, silk, and wool in red, chocolate, and purple colours. When the plants are three to four years old, the coloring matter is extracted from the root bark. The flowers are blooming at may[17].

FIG NO.1: ***Morinda coreia***

CHEMICAL CONSTITUENTS:

Morinda species are well known for the chemical diversities of anthraquinones, iridoids, saccharide fatty acid esters, and lignans. However, chemical composition differs largely depending on the part of the plants.*Morinda coreia,* known in Thai as Yo-Paa, is a tree distributed in the Southeast Asia region. It's bark and wood are used to treat fever and as an antimalarial agent in northeastern Thai (Isarn) traditional medicine. Previous studies on the chemical components of *M. coreia* reported eight iridiod glucosides, one phenolic glycoside, one secoiridoid glucoside and one anthraquinone glycosidefrom leaves and branches as well as seven anthraquinones and one anthraquinone glycoside from roots.(Table no.2)

Sl. no	Compounds	Structure	Substituents
1.	Bianthraquinone(Morindaquinone)		–
2.	i. Soranjidiol, ii. Rubiadin-1-methyl ether iii. 2-methoxy-1,3,6-trihydroxyanthraquinone iv. 1-hydroxy2-methylanthraquinone v. Tectoquinone		i. R_1=R_3=OH, R_2= H ii. R_1=OMe, R_2=OH, R_3=H iii. R_1=R_2=R_3=OH iv. R_1=OH, R_2=R_3=H v. R_1=R_2=R_3=H
3.	i. nordamnacanthal ii. damnacanthal iii. 2-formylanthraquinone		i. R_1=R_2=OH ii. R_1=OMe, R_2=OH iii. R_1=R_2=H

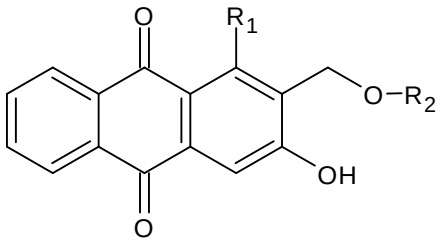
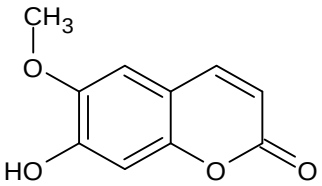
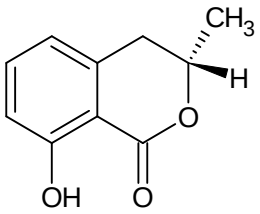
4.	i. 3-hydroxy-2-hydroxymethylanthraquinone ii. Lucidin-x-methyl ether		i. $R_1=R_2=H$ ii. $R_1=OH$, $R_2=Me$
5.	Scopoletin		–
6.	(β)-mellein		–

TABLE NO.2: Compounds structure and its constituents

M. coreia roots has resulted in the isolation of one new bianthraquinone, morindaquinone.Compound (β)-mellein was identified for the first time from the genus Morinda[18].

MAJOR PHYTOCONSTITUENTS PRESENT IN DIFFERENT PARTS

Sl.No	Phytoconstituents	Present in
1.	Ursolic acid	Leaves
2.	Anthragallol-2, 3-di-Me ether, Soranjidiol,	Root bark

	Ibericin, 6-primeveroside of morindone	
3.	Alizarin-1-Me ether, Rubiadin, D-mannitol	Stem bark[19]
4.	Quercetin, Kaempferol-3-rutinoside, Acacetine-7-glucopyranoside, Apigenin 5,7-dimethylether4'-galactoside	Leaves and Flowers[20]
5.	Damnacanthal, Nordamnacanthal (1,3-dihydroxy-2-formylanthraquinone)	Heartwood[21,22]

TABLE NO.3 Major constituents in different parts

PHARMACOLOGICAL ACTIVITY

ANTI-DIABETIC:

Diabetes mellitus, commonly known as diabetes, is a metabolic disease that causes high blood sugar. The hormone insulin moves sugar from the blood into your cells to be stored or used for energy. With diabetes, your body either doesn't make enough insulin or can't effectively use the insulin it does make.The animals fasted overnight and diabetes was induced by a single intraperitoneal injection of freshly-prepared STZ (55 mg/kg body weight of rats) in 0.1 M citrate buffer (pH 4.5). The animals were allowed to drink 5% glucose solution overnight to overcome

the drug-induced hypoglycemia. Control rats were injected with citrate buffer alone. The animals were considered as diabetic, if their blood glucose values were above 250 mg/dL on the third day after the STZ injection. The treatment was started on the fourth day after the STZ injection and this was considered the first day of treatment. The treatment was continued for 30 days.A significant increase in the level of blood glucose and a decrease in body weight were observed in diabetic rats when compared to control rats. Administration of *Morinda tinctoria* (MTR) and insulin to diabetic rats significantly decreased the level of blood glucose and increased body weight gain to near control level. The diabetic rats showed a significant decrease in the levels of total haemoglobin and asignificant increase in the level of glycosylated haemoglobin (HbA1c) and plasma insulin level as compared to diabetic rats. Administration of *Morinda tinctoria* (MTR) or insulin to diabetic rats restored the total haemoglobin and HbA1c to almost control levels[23].

ANTI-INFLAMMATORY:

Anti-inflammatory is the property of a substance that reduces inflammation or swelling. These drugs act as remedy for pain by reducing inflammation as opposed to opioids, which affect the central nervous system to block pain signaling to the brain.The protease inhibition and the prevention of protein degradation activity of AEM were measured, and the results were represented as a percentage of inhibition. About 44.10±0.26% of protease inhibition activity was exhibited by 100 µg/ml of AEM. Likely, 44.38±0.58% of inhibition of protein degradation was exhibited by AEM. The membrane stabilizing property of AEM was evaluated using red blood cells lysis assay. The results showed that the AEM stabilizes the red blood cell membrane by exhibiting about 69.36±0.20% inhibition of cell lysis.In the present study, in vitro anti-inflammatory property of M. tinctoria extract was estimated by evaluating the protease inhibition and prevention of protein denaturation properties. The results suggested that the experimental extract (AEM) was potent enough to inhibit the protease activity up to 44% and also prevent the protein degradation effectively. The membrane stabilizing property of M. tinctoria was not yet reported. The results of the current study revealed that M. tinctoria was a promising candidate to protect the membrane damages.The AEM extract comprises of quinones, steroids, terpenoids, phenols, glycosides, and tannins. The AEM showed better anti-inflammatory properties when tested in *in-vitro* models[24].

ANTI-MICROBIAL:

An antimicrobial is an agent that kills microorganisms or stops their growth including thin spores.Different concentration of n-hexane and chloroform extract of *M. coreia* was loaded onto the well and was air dried. 100 µL of the suspended H. pylori strain in PBS having McFarland 2 (1×108 CFU/mL) was spreaded and plated onto BHI medium. The well was made in the plate using well puncher and the wells were loaded with different concentrations of the extract. After 72 h of incubation, we found that the n-hexane and chloroform extract of *M. coreia* had anti-H. pylori activity showing the zone of inhibition of 7 mm at 0.4 mg/mL for n-hexane extract and 7 mm for 2.4 mg/mL chloroform extract by agar well method[25]. The antimicrobial activities in *M. coreia*have been checked against *A. niger* where the zone of inhibition was high (leaf, bark, and fruit methanol extracts). However, when *A. oryza* was used the zone of inhibition was obtained only with bark sample. Zone of inhibition was also obtained in *Salmonella* cultures against leaf methanol extract of sample[26].

ANTI-OXIDANT:

Antioxidants are compounds that protects cells from the damage caused by free radicals. Antioxidants such as thiols or ascorbic acid (vitamin C) may also act to inhibit free radical reactions.The ability of the isolate to scavenge free radicals was confirmed by estimation of its DPPH radical scavenging activity, five different concentrations (10, 50, 75, 100 and 250 µg/ml) of the pure compound were prepared. To each 3 ml of DPPH (0.1 mM/ml in ethanol) solution was added. The entire reaction mixture was incubated in complete darkness for 30 min, and thereafter, its absorbance was read at 517 nm. The results were compared with ascorbic acid, which is a standard anti-oxidant equivalent. Percentage radical scavenging (%RS) activity was calculated.The isolated compound represented significant dosage dependent antioxidant proficiency comparable to the standard antioxidant ascorbic acid. Depicts that at higher concentrations such as 250 µg/ml, the compound showed an extremely high efficiency with 94.86% radical scavenging activity and was found to be better than ascorbic acid at the same concentration (92.93%). The IC50 value for the tested compound was observed to be 75.2 µg/ml[27].

ANTI-ULCER:

Aspirin-Induced Ulcerogenesis in Pylorus Ligated Rats

Anti-ulcer is anagent that used for the prevention or treatmentof ulcers and especially ulcers of the wall of the stomach.Wistar rats of either sex weighing 180 to 250 g were divided into five groups of six animals each. Animals were placed in cages with grating floor to avoid coprophagy in fasting period.The animals were received 1% CMC (carboxy methyl cellulose) served as vehicle control + PL (pylorus ligated) andthe animals received aspirin and EEMT suspended in water and it's assigned the drug treatment for the respective 1–10 days daily. From days 8 to 10 days, animals werereceived aspirin orally as an aqueous suspension at the dose of 200 mg/kg, 2 h after the administration of the drugs. Animals were fasted for 18 h after the assigned treatment, anaesthetized, and the pylorus was ligated. The rats were sacrificed after 4 h by excess anesthesia (ether). The stomach was cut open along the greater curvature and the contents drained into small beaker, centrifuged, and then subjected to analysis for following acid secretory and biochemical parameter. The mucosa was flushed with saline and the stomach was pinned on frog board and the ulcer score was calculated[28].

WOUND HEALING:

Wound healing refers to a living organism's replacement of destroyed or damaged tissue by newly produced tissue.The animals from each group were anesthetized, the excision wound was inflicted by cutting away a 100 mm^2 skin from the shaved area Excision wound was left undressed. Topical and oral application of the plant extracts to the divided groups viz. Control, Test-Oral, and Test-Local, respectively, were done once daily until the wound healed completely. Wound contraction and epithelialization period of control and experimental wounds were monitored and determined.This study has providesdinformation about the wound healing efficacy of an aqueous extract of *M. tinctoria*Roxb leaves. The results suggests that the efficacy of *M. tinctoria* Roxb aqueous leaf extract as a wound healing agent and can also be used as a therapeutic agent for internal as well as external wounds[29].

LARVICIDAL:

A larvicide is an insecticide that is specifically targeted against the larval life stage of an insect. Their most common use is against mosquitoes.The larvicidal activity was assessed by the

standard procedure of WHO. Twenty-five 3rd instar larvae of Ae. aegypti were transferred separately from culture being maintained in the laboratory to the 250 ml beaker containing the 100 ml of desired concentration of plant extracts and AgNps respectively. The control was set up with dechlorinated tap water. The moribund larvae were counted,has been reported that the absorption spectra of AgNps were highly symmetric single band absorption with peak at 421 nm.Third instar larvae of Ae. aegypti was treated with biosynthesized silver nanoparticles and the percentage mortality was assessed against various concentrations ranging between (0.5-7 ppm). The LC50 value of synthesized AgNps was 3.631 ppm. The low release rate of nanoemulsion with large droplets size that resulted in prolonged mosquito repellent activity compared to the nanoemulsion with small droplets. The acetone extract of *M. tinctoria* was tested for its efficiency against third instar larvae of Ae. aegypti. The larvae were subjected to different concentrations (2-24 ppm) of the leaf extract and 11.716 ppm was recorded as LC50 value. In these studies, envisaged that the Indian marine algae extracts possessed potential larvicidal activity. Aqueousextract of *Morinda coreia*was found to exhibit, a strong antimosquito activity as evident from its ability to inflict 100% mortality of all the developmental stage of Ae. Aegypti[30].

ANTI-CANCER:

Cancer is an abnormal growth of cells which tends to proliferate in an uncontrolled way, the anti-cancer drug either kill cancer cells or modify their growth.The ultrafiltered protein fractions were tested for cytotoxic activity against the selected cancer cell lines using MTT assay. Different concentrations of ultrafiltered proteins ranging from 2 to 100 µg/ml were added to each well of 96 well plates. The cells were cultured in 96-well plates in DMEM supplemented with 10% FBS for 24 h. After 24 h the cells were observed under phase contrast microscope and morphology of cells were observed. The medium containing positive control and test samples were removed. MTT (50 µl) dye was added to the wells containing 200 µl of fresh medium. The cell lines were incubated in CO2 incubator for 4 h. After 4 h of incubation, medium containing dye was removed and 200 µl of DMSO was added to dissolve the formazan crystal. The absorbance was recorded at 570 nm and the percentage of cell viability was calculated.However, the DNA extracted from the untreated Vero cells, appeared as distinct band showing the*M. pubescens* can act as potential anticancer agents in cancer chemotherapy[31].

The methanol extract of the leaves of *Morinda tinctoria*Roxb. (MEMT) was studied for its anticancer activity using *in-vitro* and *in-vivo* cancer models. MEMT was investigated for its short-term cytotoxicity on EAC tumor cells by trypan blue dye exclusion method and *in-vitro* cytotoxicity on NIH 3T3, A549, Hep2 and HepG2 cells by MTT assay. Anticancer activity was monitored. 5-Fluorouracil was used as a standard. The extract showed potent in vitro cytotoxicity against each of the tested tumor cell lines, but it was found to be harmless to normal cells (MEMT at the dose of 200 and 400 mg/kg). The results showed a significant anticancer and cytotoxic effect of MEMT against EAC and human cancer cell lines, and thus supported the ethnomedical use of *Morinda tinctoria*[32].

DOCKING STUDY

Molecular docking is a computational tool that can predict how a ligand will attach to a protein with a known three-dimensional structure. Docking may be used to do computergenerated screening on enormous collections of compounds, rate the outcomes, and offer structural models for in what manner the ligands inhibit the target, which is tremendously beneficial in the search for new inhibitors. There is no literature available about molecular docking studies describing the interaction of *Rubiadin*with molecular targets involved in cancer development. To circumvent this constraint, we employed protein-ligand molecular docking to assess the *Rubiadin's* binding mechanism and interaction energy with four important enzyme targets, which were identified in this research as being responsible for variety of cancers.

A number of cancer treatments have been evaluated in clinical trials to see if they can inhibit the cMET receptor tyrosine kinase, and resistance mutations in the cMET gene are beginning to be identified in a number of these medications. Molecular investigations are still required to further understand individual cMET modifications at the molecular level, particularly in terms of small molecule identification[33]. In certain cancers, chromosomal translocation, amplification, or point mutations in the anaplastic lymphoma kinase (ALK) gene cause the tyrosine kinase to be constitutively activated. This gene has been found as a potential target for molecular docking studies, and it will be investigated extensively[34]. PI5P4Ks have been shown to play a role in the growth of cancer cells as well as the development of other disorders. Due to a lack of effective and selective small drugs on the market, targeting these kinases for therapeutic purposes has

gotten little attention[35].Hsp90 and Hsp90 have been linked to cancer and neurological disorders, although determining their precise role in these diseases has been difficult due to a lack of specific pharmacological studies[36]. The protein with the PDB IDs 3AOX, 6OLX, 6OSP, and 6SDC were extracted from the protein data bank to commemorate the above four targets. Molegro Virtual Docker (MVD) 6.0 was used to conduct the molecular docking study[37].

CANCER TARGETED PROTEINS:

The docking procedure includes the following steps. MVD was used to import the molecules, including protein and ligand (*Rubiadin*). In the protein molecule, potential binding sites and the configuration of the search space were determined. The Docking Wizard was used to run a docking simulation. The Pose Organizer and the ligand energy inspector tool were used to inspect the docking results, and the results were tabulated and the docked view was extracted. The MolDock score with the lowest values was discovered to have the highest binding affinity to the target proteins. *Rubiadin* affinity for cancer targets was found to be 6SDC>6OLX>3AOX>6OSP (Table no.4), according to the report obtained. This result strengthens the anticancer potential of *Rubiadin* and that could help to enlighten this biologically active compound to the next level of drug discovery and development.

SOFTWARES USED FOR DOCKING:

- Molegro Virtual Docker (MVD) 6.0 - import the molecules
- Docking Wizard - used to run a docking simulation
- The Pose Organizer - were used to inspect the docking results
- Ligand energy inspector tool - were used to inspect the docking results

Requirements:

- Ligand: Rubiadin (Fig no.2)
- Protein (Cancer targeted proteins): 3AOX, 6OLX, 6OSP, and 6SDC (Fig no.3)

LIGAND:

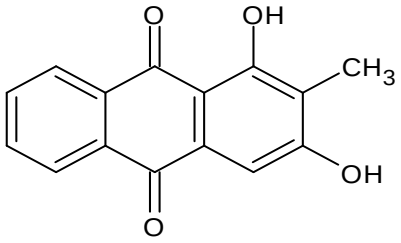
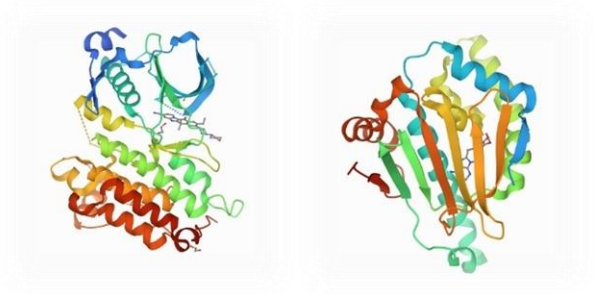
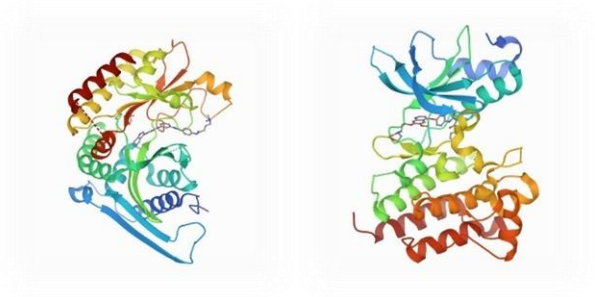


Fig no.2: Structure of Rubiadin (Ligand)

CANCER TARGETED PROTEINS



3AOX6OLX



6OSP 6SDC

Fig no.3: Cancer targeted proteins

RUBIADIN AFFINITY TOWARDS CANCER TARGETS

SL.NO	PROTEINS	LIGAND	MOL.DOCK SCORE
1.	6SDC	Rubiadin	-96.066
2.	6OLX	Rubiadin	-87.933
3.	3AOX	Rubiadin	-76.181
4.	6OSP	Rubiadin	-72.106

TABLE NO.4: Docking Score

From this table no.4, we can conclude that the lower molecular dock score = The higher binding

affinity to the target cancer protein. Binding affinity was **6SDC>6OLX>3AOX>6OSP** which was found. The docked view is given below 3AOX(Fig no.4), 6OLX (Fig no.5), 6OSP (Fig no.6), 6SDC (Fig no.7)[38].

DOCKED VIEW:

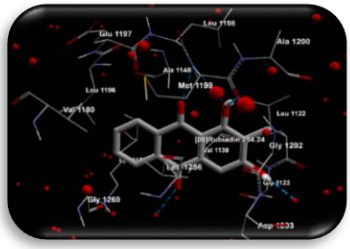


Fig no.4: 3AOX

Amino acid residue: Ala 1148, Ala 1200, Asp 1203, Glu 1197, Gly 1123, Gly 1202, Gly 1269, Leu 1122, Leu 1196, Leu 1198, Leu 1256, Lys 1150, Met 1199, Val 1130, Val 1180, water 60, 77, 121, 149, 175.

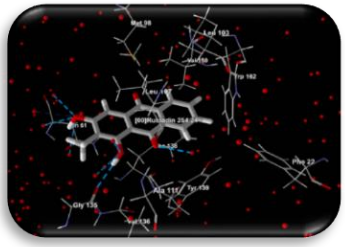


Fig no.5: 6OLX

Amino acid residue: Ala 111, Asn 51, Gly 135, Leu 103, Leu 107, Met 98, Phe 22, Phe 138, Trp 162, Tyr 139, Val 136, Val 150, water 34, 55, 82, 89, 112, 132, 141, 161, 179, 180, 266, 307, 336, 347.

.

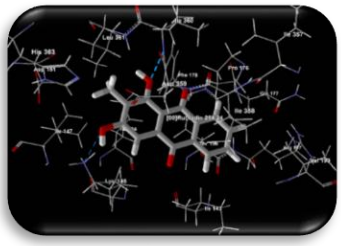


Fig no.6: 6OSP

Amino acid residue: Arg 197, Asp 151, Asp 359, Gln 177, His 363, Ile 143, Ile 147, Ile 194, Ile 357, Ile 358, Ile 360, Leu 361, Lys 145, Phe 178, Pro 176, Thr 196, Val 199.

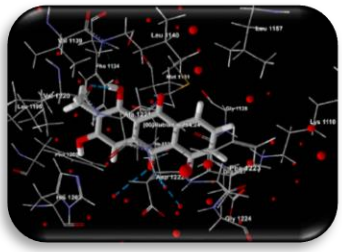


Fig no.7: 6SDC

Amino acid residue: Ala 1221, Asp 1222, Glu 1127, Gly 1128, Gly 1224, His 1202, Ile 1130, Leu 1140, Leu 1157, Leu 1195, Lys 1110, Met 1131, Phe 1134, Phe 1200, Phe 1223, Val 1139, Val 1220, water 24, 38, 86, 195, 227, 259.

Inhibitor of human dihydrofolate reductase enzyme (DHFR):

Dihydrofolate reductase (DHFR) plays a vital role in the DNA synthesis by reducing dihydrofolic acid to tetrahydrofolic acid which is an essential component for nucleotide biosynthesis. DHFR has been an attractive target for chemotherapy of many diseases including cancer. Synthetic ligands like methotrexate (MTX), act as potential anti-metabolites by

mimicking the substrate dihydrofolic acid (DHFA) they inhibit the activity of DHFR antagonistically. In this study, molecular docking and in silico studies were carried out in an attempt to evaluate the drug candidature of some antraquinones, (damnacanthal, nor-damnacanthal, morindone, rubiadin, and Lucidin) as inhibitors of human dihydrofolate reductase enzyme, in order to develop better antifolates drugs. The molecular docking study suggested that these compounds can act as a putative inhibitor of hDHFR. The docked Rubiadin with hDHFR is shown in the (Fig.no.8)[39].

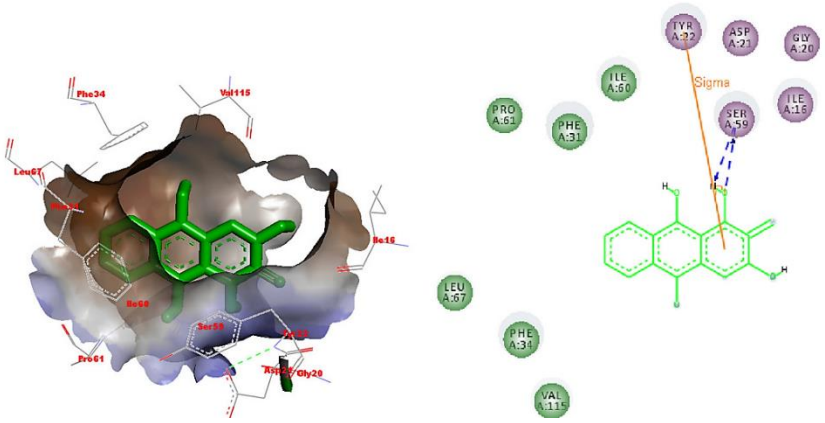


Fig.no.8 Rubiadin docked with hDHFR

Rubiadin Dock score: -8.6

Rubiadin showed a hydrogen bond with ASN 64(A), LEU 67(A), LYS 68(A), ARG 70(A) and Van der wall interaction with GLN 35 (A), ASN 64(A), and LYS 68(A).

Rubiadin interaction with α-amylase and α-glucosidase:

In order to understand the mechanism and interaction of rubiadin as anti-diabetic agent, docking studies were implemented on two enzymes viz. α-amylase and α-glucosidase. The docking score and ligand-receptor interactions of rubiadin receptor complex generated after docking. Rubiadin displayed docking score of −6.62 with α-amylase which means it fts well in the receptor and can act as an inhibitor; it also displayed good ligand-receptor interactions with an important amino acid such as TRP59, TYR62, and Glu233. The drug displayed a docking score of −4.47 with α-glucosidase, which signifies that rubiadin has α-glucosidase inhibitory potential, but it is not as potent as acarbose. The results of molecular docking confirmed the binding by the enzymatic

inhibition mechanisms of rubiadin to active sites of α-amylase and α-glucosidase[40].

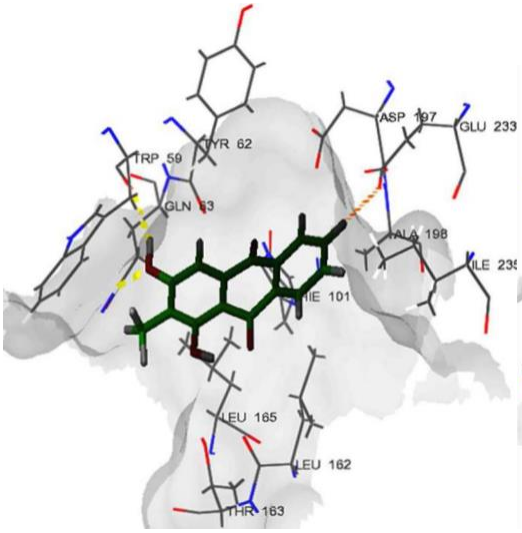


Fig.no.9

Rubiadin interactions with α-amylase (Docking Score-6.62)

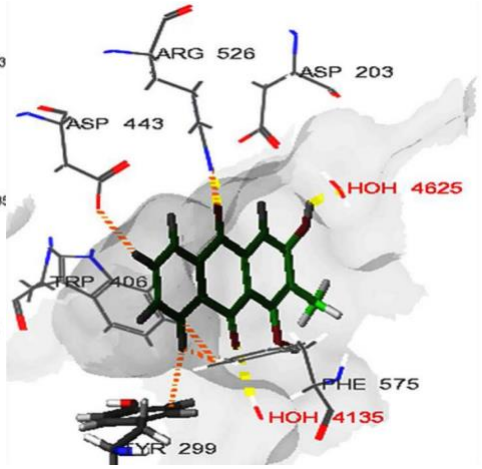


Fig.no.10

Rubiadin interactions with α-glucosidase (Docking score −4.47)

CONCLUSION:

In this review of literature on *Morinda coreia* was examined by different articles. Based on the information gathered, there has been manychemical constituents and activities had found on different parts of *Morinda coreia*. The docking studies had been done only on the chemical compound *rubiadin* found in *Rubia cortifolia*.*Rubiadin* is one of chemical constituentwhich is found in *Morinda coreia*.It has been found that in bark part of *Morinda coreia* pharmacological activity has not been done. So, the further research and docking studies will be done on the bark partof *Morinda coreia*.

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