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A Study on *In-Silico* Supported Nephroprotective Action of *Coccinia* Species

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ABSTRACT

There are many health problems that can be addressed using medicinal plants. The healthcare system often utilizes herbal remedies, with one particularly important plant being the *Coccinia* species. This plant has historically been used by various tribes as a treatment for diseases. The species has been shown to possess numerous helpful assets, counting antibacterial, analgesic, antispasmodic, anti-inflammatory, antipyretic, cathartic, and expectorant properties. Chemical components such as alkaloids, glycosides, triterpenoids, phenols, flavonoids, saponins, and tannins can be found in this species. The aim of the present investigation was to isolate, purify, and identify active chemical complex from the leaves of the *Coccinia grandis*. The extraction process involved consuming Soxhlet apparatus to extract the leaves. Numerous phytochemical tests were conducted, and both TLC and column chromatography were used to isolate the compound. The isolated compounds were further characterized through UV, IR and analysis. The nephroprotective activity of the compound was then evaluated in an in vitro model.

Keywords: *Coccinia grandis*; Nephroprotective activity; Molecular docking

INTRODUCTION

The new year brings worldwide interest in the research and use of traditional medicine. Therefore, governments are trying to cooperate to identify and use effective and efficient medicines in national health systems. Since ancient times, people have studied nature, especially plant, to find new medicines, which has led to the use of traditional medicine, many species of plants effective in treating various diseases. In India, about 95% of traditional medicine is like this. Unani, Ayurveda, Homeopathy and Sadhana are herbs. Plants produce primary and secondary metabolites with different functions. *Coccinia* is a plant from the Cucurbitaceae family. It is in Central Africa, Asia and India. It is a perennial climbing plant that can be propagated vegetative from seeds. Seeds can be an excellent source of oil and protein that can meet the needs of the market and the consumer. The stalks are either perennially thin climbers or herbaceous climbers, and occasionally, adventitious roots sprout along ground. Branches are long, taut and flexible and can wrap around the entire length of the host. Its leaves are arranged together, its flowers are large, star shaped, white, and its fruit is dark red (Figure 1). The leaves and fruits that were used in foods [1-5].



Figure 1: *Coccinia grandis* A) Leaf B) Flower C) Fruit.

Coccinia grandis (ivy gourd) is rarely grown as a garden vegetable in tropical and subtropical climates worldwide. Its homeland is thought to be Central Africa, India and Asia. Its long history of human use, cultivation, and transportation obscures its origins. It is a plant species that grows in Southeast Asia. Urolithiasis is the formation of calculi, or condition associated with urinary calculi. The term calculi are synonymous with uroliths, stones, or crystals. These calculi are formed by deposits of polycrystalline aggregates composed of varied amount of crystalloid and organic matrix. Common components of calculi include calcium oxalate (pure), calcium oxalate in combination with aspartate, uric acid (pure), calcium oxalate in combination with uric acid, calcium oxalate dihydrate in combination calcium phosphate. In this present study three plants are selected for the anti urolithiasis study [6-9].

Nephrotoxicity is caused by regular intake of certain drugs. In this case, the kidneys will not be able to clear excess urine and waste products. The kidney is an important organ that helps the body eliminates waste and toxins. Kidney failure is a disease in which harmful metabolites are present in the body and causes serious consequences such as liver enlargement, edema and ascites. The glomerular filtration rate is about 125 ml/minute and the blood flow to the kidney is about 625 ml/minute. As a result, the kidneys receive around four times as much blood as other organs. The glomerular filtration in the nephron's Bowman capsule filters at a rate of around 125 milliliters per minute, therefore the kidney filters approximately 180 L of blood every day [10].

MATERIALS AND METHOD

The whole plant of *Coccinia Grandis* was collected in the month of Jan 2023 from Bhalwani, Pandharpur, Dist Solapur, India. The plant material was authenticated at Padabhushan Vasant Rao Patil Mahavidyalaya, Kavathemahankal, Dist-Sangli [11-15].

Extraction

About 2 kg of shade dried plant leaves of *Coccinia grandis* extracted in Soxhlet successively extracted with n-hexane, chloroform, ethyl acetate and methanol. Each extract was evaporated by using rotary vacuum evaporator. The extract obtained with each solvent was weighed and the percentage yield was calculated in terms of dried weight of the plant leaves. The consistency and colour of the extract were noted. All the solvents used for this work were of analytical grade (Table 1). The n-hexane, chloroform, ethyl acetate, methanol extracts of the leaf powder of *Coccinia grandis* stem were subjected to qualitative chemical analysis [16].

Table 1: The percentage yield of successive extracts of the leaves of *Coccinia grandis*.

Sr.no	Extract	Colour	Physical nature	Percentage yield (w/w)
1	n-Hexane	Green/Sticky mass	Waxy Semisolid	1.8
2	Chloroform	Green/Sticky mass	Semisolid	2
3	Ethyl Acetate	Brownish green solid	Solid	3.4
4	Methanol	Brownish green solid	Solid	7.9

RESULTS

Qualitative chemical examination of plant-based constituents in *Coccinia grandis* leaf extracts as shown in Table 2 [17].

Table 2: Phytochemical screening of *Coccinia grandis*.

Sr.no	Test	n-Hexane	Chloroform	Ethyl acetate	Methanol
1	Alkaloids	-	-	+	-
2	Carbohydrate	-	-	+	-
3	Glycosides	-	+	-	+
4	Phytosterol	-	-	-	+
5	Fixed oils and Fats	-	-	-	-
6	Tannins	-	-	-	-
7	Phenols	-	-		+
8	Proteins	-	-	+	-
9	Gums and Mucilages	-	-	-	-
10	Flavonoids	-	-	-	+
11	Terpenoids	-	-	-	+
12	Steroids	-	+	-	-
13	Saponins	-	-	+	+
Note: +ve indicates positive result; whereas -ve indicates negative result					

Qualitative preliminary phytochemical analysis of *Coccinia grandis* was performed initially with different chemical reagents to detect the nature of phytoconstituents and their presence in each extract (Table 3 and Figure 2).

Thin layer chromatography

Table 3: The TLC studies of methanol extracts of *Coccinia grandis*.

S.no	Name of the Extract	Solvent system	No of spots	R _f Values
1	Methanol (CGM)	Methanol : Ethyl acetate: Water (6:3:1)	1	0.33

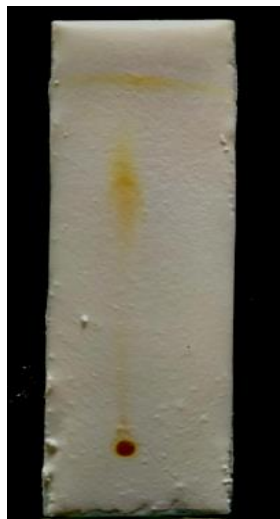


Figure 2: TLC of isolated compound.

Column chromatography

The Figure 3 show the column chromatography of a) Chloroform b) Methanol c) n-Hexane extract.



Figure 3: Column chromatography of a) Chloroform b) Methanol c) n-Hexane extract.

- Adsorbent: Silica for column chromatography activated at 110°C for 1 hour
- Length of column: 40 cm
- Length of adsorbent: 25 cm

UV spectrum: Fraction in pet methanol

The UV spectrum show in Figure 4.

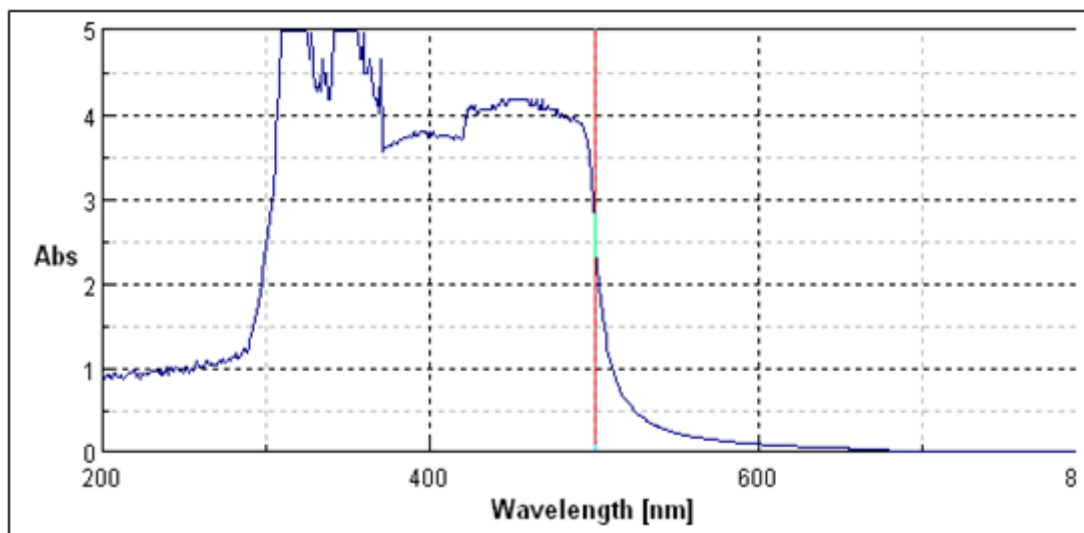


Figure 4: The UV spectrum showed characteristic bands of fraction in methanol at $\lambda = 352$.

The UV spectra of isolated cextract from *Coccinia grandis* was performed using methanol. The UV spectrum showed characteristic bands of fraction in methanol at $\lambda = 321, 352, 413$. The UV spectra of standard showed one characteristic peak at $\lambda = 352$ (Figure 5 and Table 4).

FTIR of *Coccinia grandis* extract

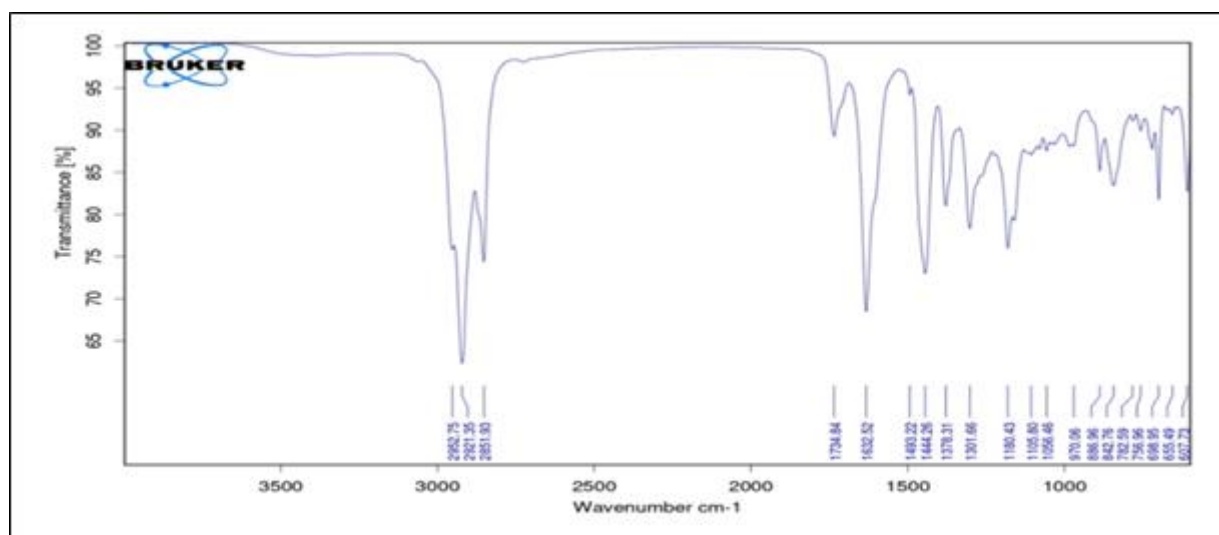


Figure 5: FTIR Spectrum of *Coccinia grandis* extract.

Table 4: FTIR Spectrum analysis.

Sr.no.	Peak values	Bonds	Functional groups
1	2952.75	O–H stretch, H–bonded	Alcohols, Phenols
2	2921.35	C–H stretch	Alkanes
3	1493.22	C–C stretch (in–ring)	Aromatics
4	1378.31	C–O stretch	Alcohols
5	842.46, 698.95	C–H “oop”	Aromatics

In-Vitro nephroprotective assay

NRK 52 E Cell line (Normal Kidney Cell Line)

The result show in Table 5 and Figures 6-8

Table 5: Effect of compound against NRK52E Cell line.

Sr.no	Sample code	Conc.($\mu\text{g/ml}$)	OD			Mean	% Of inhibition	% Of viability	IC50 ($\mu\text{g/ml}$)
1	Control		1.532			-	-	-	-
2	Standard	20	1.453	1.452	1.454	1.453	5.15%	94.84%	NE
	(5,Flurour - acil)	40	1.397	1.396	1.395	1.396	8.87%	91.13%	
		60	1.386	1.387	1.388	1.387	9.46%	90.54%	
		80	1.369	1.368	1.369	1.368	10.70%	89.30%	
		100	1.35	1.352	1.35	1.35	11.87%	88.12%	
3	CG1	20	1.37	1.371	1.372	1.371	10.50%	89.50%	NE
		40	1.342	1.341	1.34	1.341	12.46%	87.54%	
		60	1.287	1.286	1.285	1.286	16.05%	83.95%	
		80	1.26	1.262	1.26	1.26	17.75%	82.25%	
		100	1.215	1.214	1.213	1.214	20.75%	79.25%	

*NE-Not Evaluable

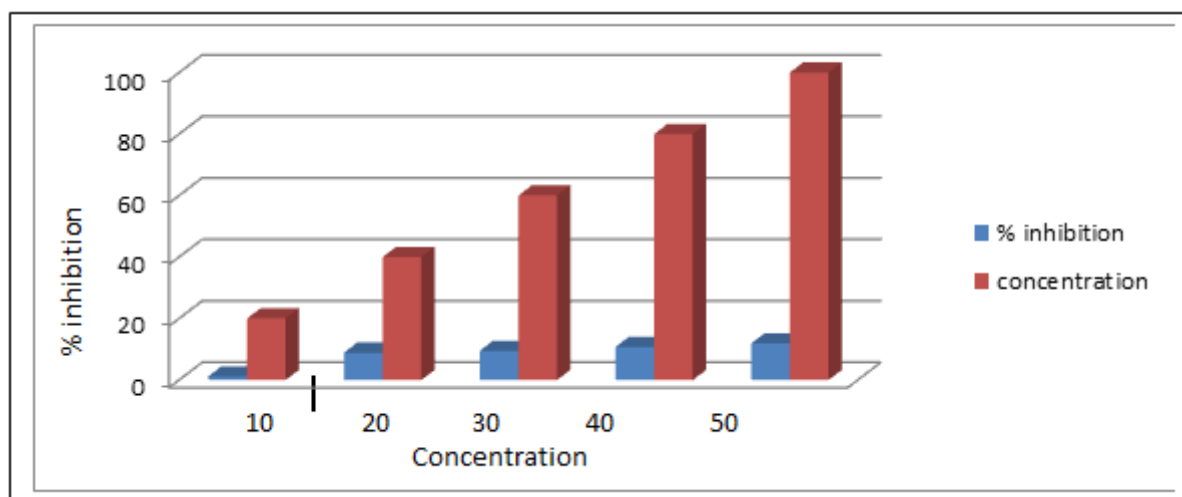
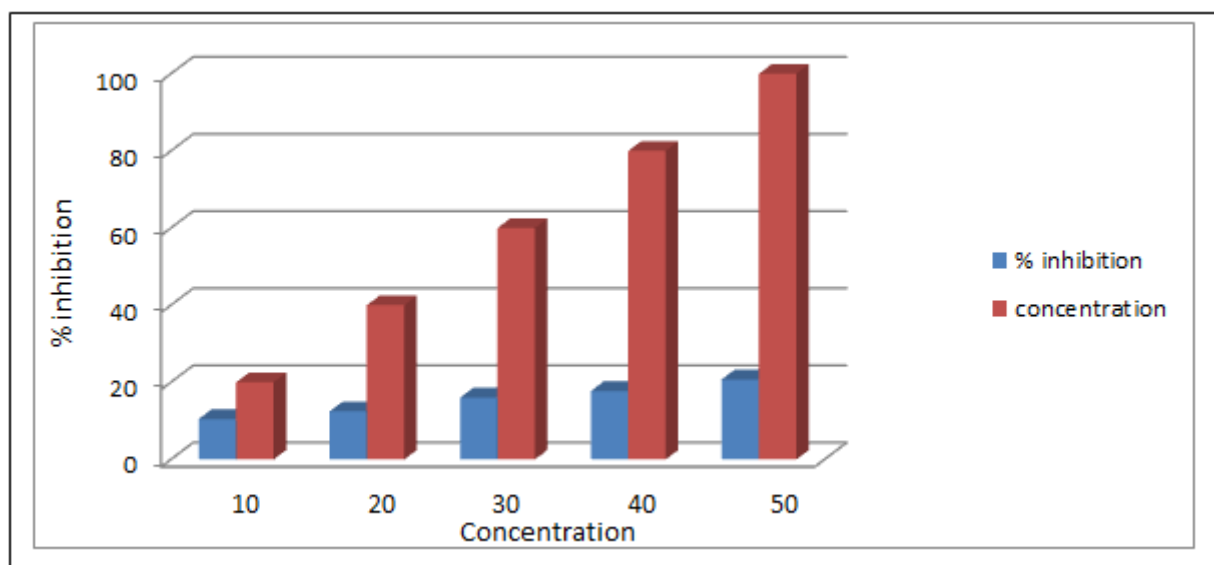


Figure 6: Graphical representation of anti-nephroprotective Standard.

Figure 7: Graphical representation of anti-nephroprotective methanolic extract of *Coccinia grandis*.

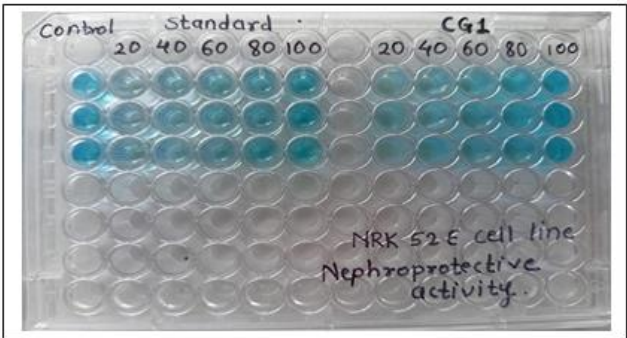


Figure 8: NRK S2E cell line nephroprotective activity.

At the different Concentrations Sample Code CG1 shows low percent of inhibition and against NRK S2E (Kidney Cells) cell line versus a typical medication 5FU. On basis of percent of viability we can conclude that the sample CG1 may not harm the normal kidney cell lines and it may protect the kidney from the harm organ damages [18].

In-silico study

Investigation of protein 1V97 is done by using PDB sum software with the help of Ramchandran plot procheck analysis. According to Ramchandran plot statistics for 1V97 protein the most favoured regions is 88.7%, additional allowed region is 10.3% generally allowed region is 0.6% and disallowed region is 0.4% which are shown in Figures 9 and 10 [19].

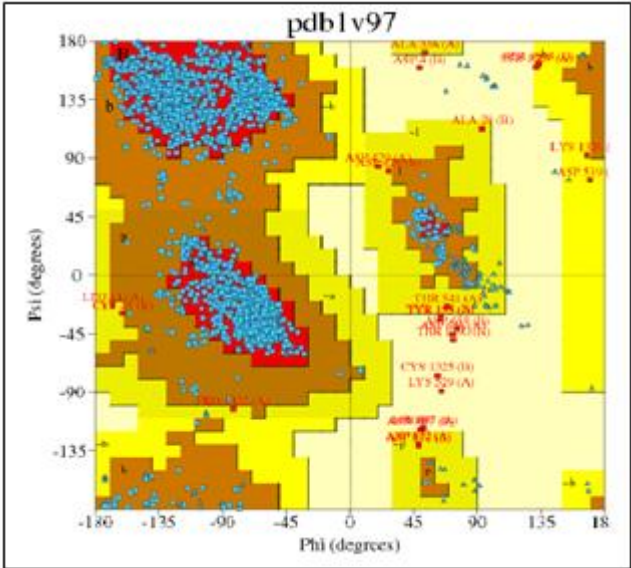


Figure 9: Ramchandran plot of 1V97.

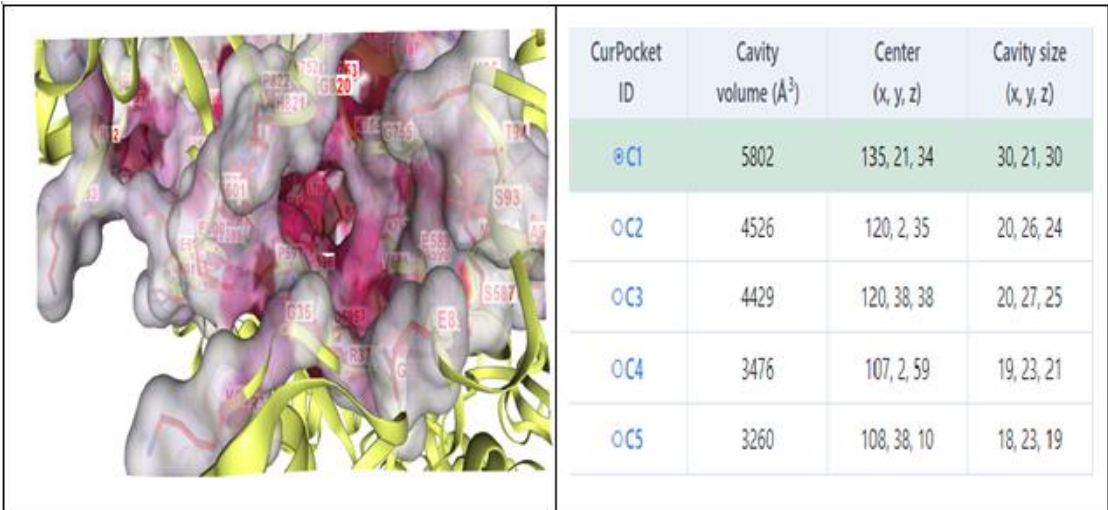


Figure 10: Cavity detection of protein 1V9.

All data obtained from molecular docking of both proteins with ligands are depicted in Tables 6-9 and Figures 11-15 [20].

Table 6: Lipinski properties of bioactive compounds from *C. grandis* leaves.

S. no.	Compound name	Molecular weight	Log p	H-bond donar	H-bond acceptor	Molar refractivity
1	Betasitosterol	414.71 g/mol	4.79	1	1	133.23
2	Cucurbitacin B	558.70 g/mol	1.46	3	8	150.94
3	Kaempferol	286.24 g/mol	1.47	4	6	76.01
4	Thiamine	265.35 g/mol	-1.6	2	3	73.12
5	Ferulic acid	194.18 g/mol	1.62	2	4	51.63
6	Quercetin	302.24 g/mol	1.63	5	7	78.03
7	Ombium	330.29 g/mol	2.83	3	7	51.63
8	Ascorbic acid	176.12 g/mol	0.39	4	6	35.12
9	Trans pcoumaric acid	164.16 g/mol	0.95	2	3	45.13
10	Carbonic Acid	62.02 g/mol	-0.22	2	3	10.65

Table 7: ADME properties of various bioactive compounds.

S. no	Compound name	Formula	Distribution	Absorption				Toxicity
			BBB Permeability	GI Absorption	Human intestinal absorption	Skin permeability	CACO-2 Permeability	Toxicity predicted LD 50
1	Betasitosterol	C ₂₉ H ₅₀ O	0.781	Low	94.464	-2.783	1.201	2.552
2	Cucurbitacin B	C ₃₂ H ₄₆ O ₈	-1.003	Low	89.52	-3.496	0.588	2.381
3	kaempferol	C ₁₅ H ₁₀ O ₆	-0.939	High	74.29	-2.735	0.032	2.449
4	Thiamine	C ₁₂ H ₁₇ N ₄ O ₅	-0.368	High	100	-2.792	0.867	2.672
5	Ferulic acid	C ₁₀ H ₁₀ O ₄	-0.239	High	93.685	-2.72	0.176	2.282
6	Quercetin	C ₁₅ H ₁₀ O ₇	-1.098	High	77.207	-2.735	-0.229	2.471
7	Ombiun	C ₁₇ H ₁₄ O ₇	-1.089	High	87.47	-2.735	0.402	2.272
8	Ascorbic acid	C ₅ H ₈ O ₆	-0.985	High	39.154	-2.955	-0.255	1.063
9	trans p coumaric acid	C ₉ H ₈ O ₃	-0.225	High	93.494	-2.715	1.21	2.155
10	Carbonic ssacid	CH ₂ O ₃	-0.428	High	83.064	-2.737	1.12	1.439
11	Niacin	C ₆ H ₂ ON ₄ O ₆	-0.323	High	94.099	-2.735	1.17	2.24

Table 8: Moleculardocknig result examination of bioactive substances of *coccinia grandis* against the protein 1UZE.

Compound Name	Binding affinity (kcl/mol)	Conventional H-bond Interaction	Pi Sigma Interaction	Pi Alkyl interaction	Van-der-Waals interaction	Other interaction
Betasitosterol	-9.3	GLU 411	-	VAL518,LEU81,LEU140 , LEU139	GLU143,TYR 69, ASN70, ASN 66, VAL351,ASN 136, ASN85 ARG124, SER516, TRP357, SER355, TYR523	-
Cucurbitacin B	-10	ILE 204, ASN211, GLU124	-	-	ALA 207, TRP220, TYR135, LEU139, SER219,	-

					ALA208	
Kaempferol	-8.2	ASP415, TYR520, LYS511, GLN281, ASP377	VAL380	ALA 354	GLN369, GLU162, HIS353, HIS513, PHE457, TYR523, PHE527, HIS383	-
Thiamine	-6.9	TYR 62, SER 355	-	- LEU 82, LEU 139, LEU 81, LEU 140	TYR 69, VAL 351, TRP 357, GLU 143, ASN 70, PHE 512, VAL 518, ASN 85, ASN 136	Other C-H bond- LYS 368, SER 516
Ferulic Acid	-6.5	ARG 124, SER 517	-	ILE 204, ALA 207	LEU 139, TYR 135, SER 219, TYR 213, ASP 121, ALA 208	Other Pi-anion- GLU123 Amide- pistacked -TRP 220
Quercetin	-8.3	THR 301, ASP 453	-	LYS 449, LEU 375	THR 302, ASP 300, MET 299, LEU 433, SER 298, GIU 376, VAL 379, MET 450, SER 284, ASN 285	-
Ombiun	-8.5	GLY 404, GLU 384, TYR 523, ARG 522	-	MET 223, PRO 407, PHE 512, HIS 353, VAL 518	ASN 406, PHE 391, ALA 356, SER 355	Other Pi-cation- GLU 411 Pi- Anion- GLU 403C-H bond HIS 410, HIS 387, HIS 513
Ascorbic acid	-5.7	ASP 121, TRP 220	-	-	TYR 213, ALA 208, ALA 207, ILE 204, ARG 124, TYR 135, GLU 123, ASN 211, SER 219	
trans p coumaric acid	-6.2	ARG 124, SER 517	-	ALA 207	LEU 139, TYR 135, SER 219, ASP 121, TYR 213, ASN 211, TRP 220, ILE 204	Other Pi-anion- GLU 123
Carbonic Acid	-3.3	HIS 353, CYS 352, SER 147, VAL 350	-	-	PHE 512, VAL 351, LEU 161, TYR 146	-
Niacin	-5.4	ASN 85, ARG 124	-	- LEU 139	LEU 81, TYR 62, ASN 136, LEU 140, GLU 143	-
Quercetin	-8.3	THR 301, ASP 453	-	LYS 449, LEU 375	THR 302, ASP 300, MET 299, LEU 433, SER 298, GIU 376, VAL 379,	-

					MET 450,SER 284, ASN 285	
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Table 9: Drug likeliness propertiesof isolated ligand from *coccinia grandi*.

Sr. no.	Compound	Lipinski	Ghose	Veber	Egan	Muegge
1	Betasitosterol	Yes	No	Yes	No	No
2	Cucurbitacin B	Yes	No	Yes	No	Yes
3	Kaempferol	Yes	Yes	Yes	Yes	Yes
4	Thiamine	Yes	Yes	Yes	Yes	Yes
5	Ferulic Acid	Yes	Yes	Yes	Yes	No
6	Quercetin	Yes	Yes	Yes	Yes	Yes
7	Ombium	Yes	Yes	Yes	Yes	Yes
8	Ascorbic acid	Yes	No	Yes	Yes	No
9	Trans p coumaric acid	Yes	Yes	Yes	Yes	No
10	Carbonic Acid	Yes	No	Yes	Yes	No
11	Niacin	Yes	No	Yes	Yes	No

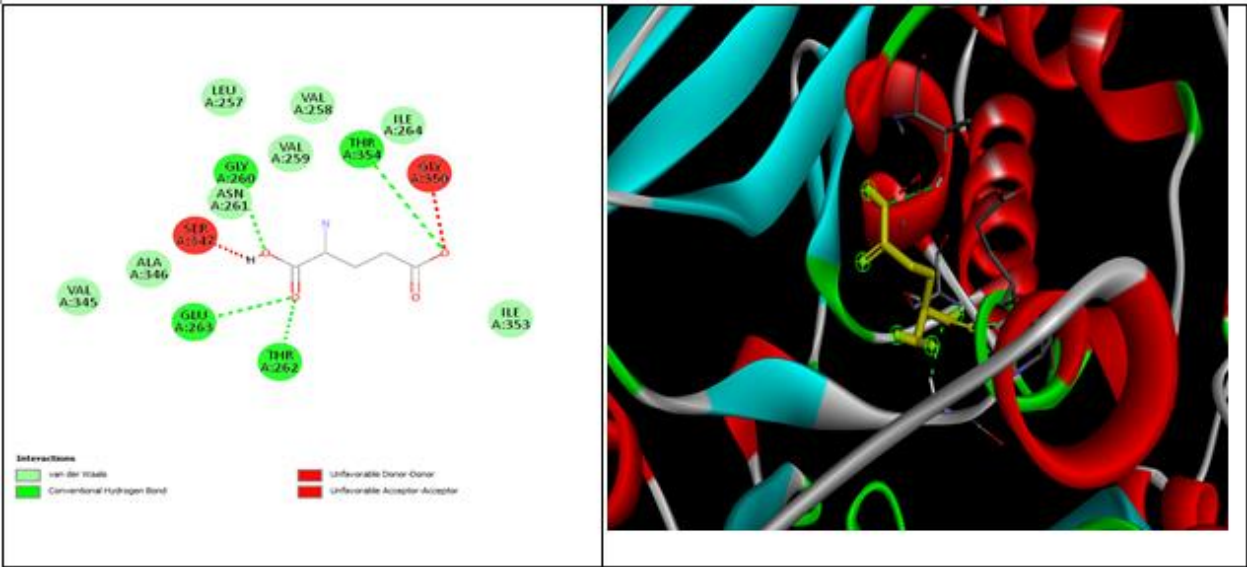


Figure 11: C.2D and 3D interactions of cucurbitacin B against receptor 1V97.

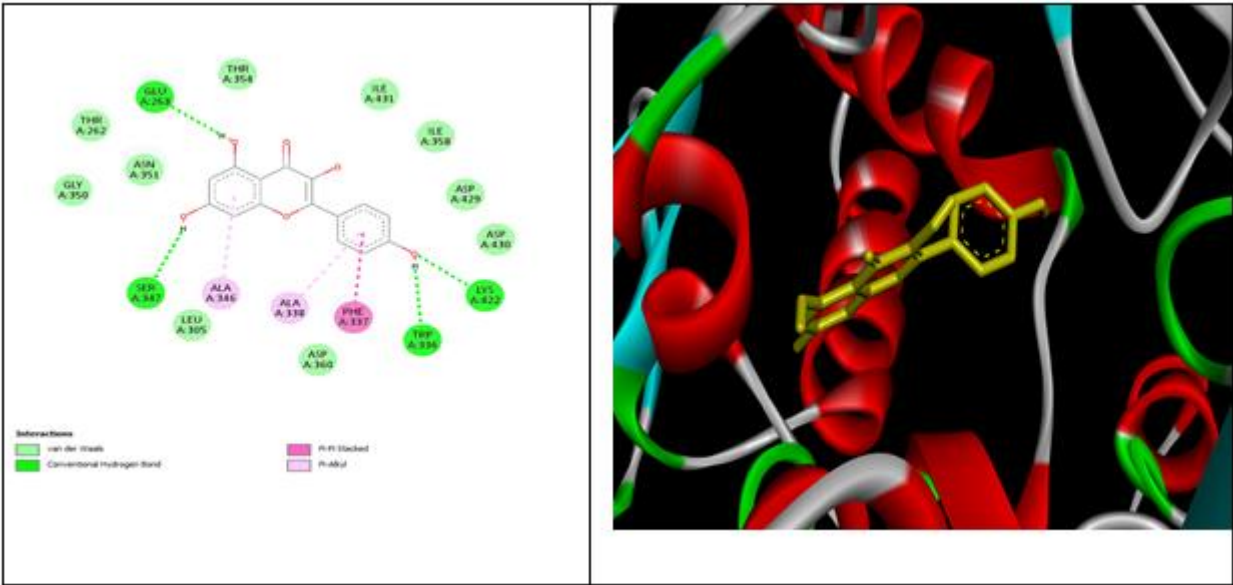
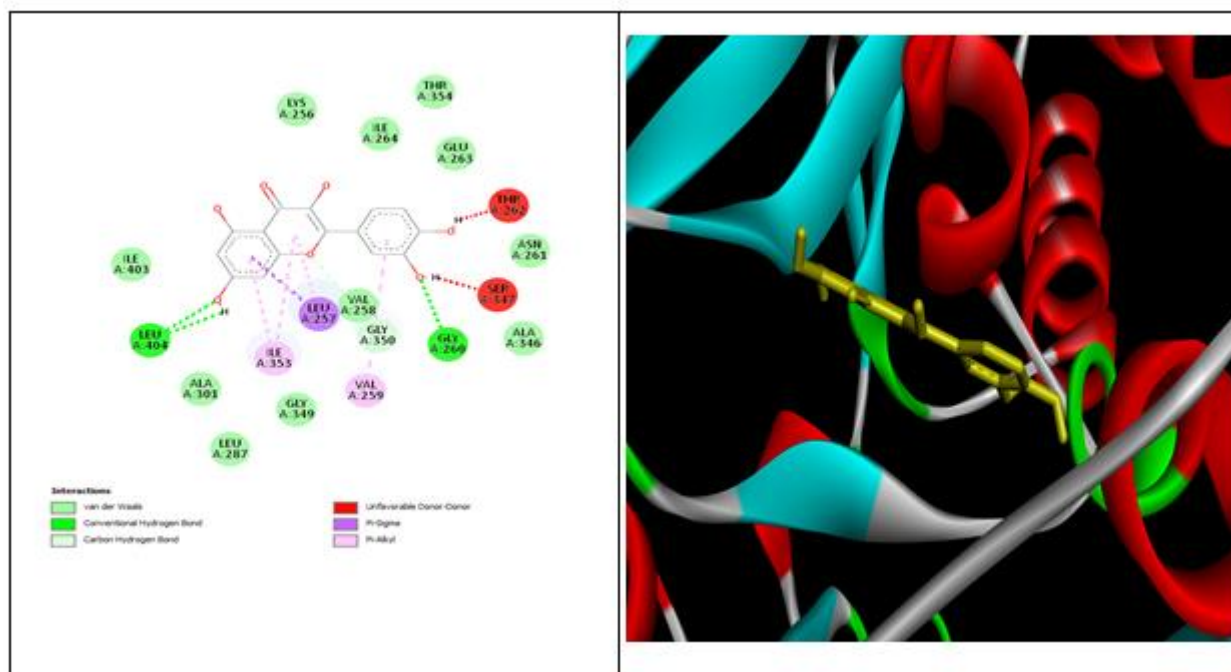
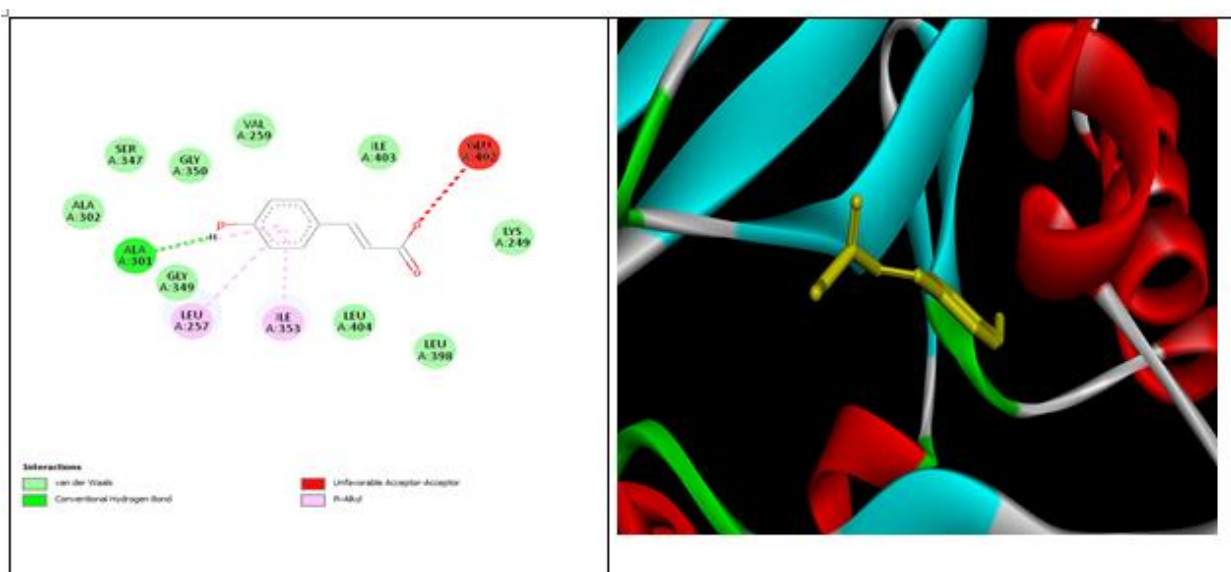


Figure 12: E.2D and 3D interactions of Kaempferol against receptor 1V97.**Figure 13:** G. 2D and 3D interactions of ferulic acid against receptor 1V97.**Figure 14:** I.2D and 3D interactions of quercetin against receptor 1V9.

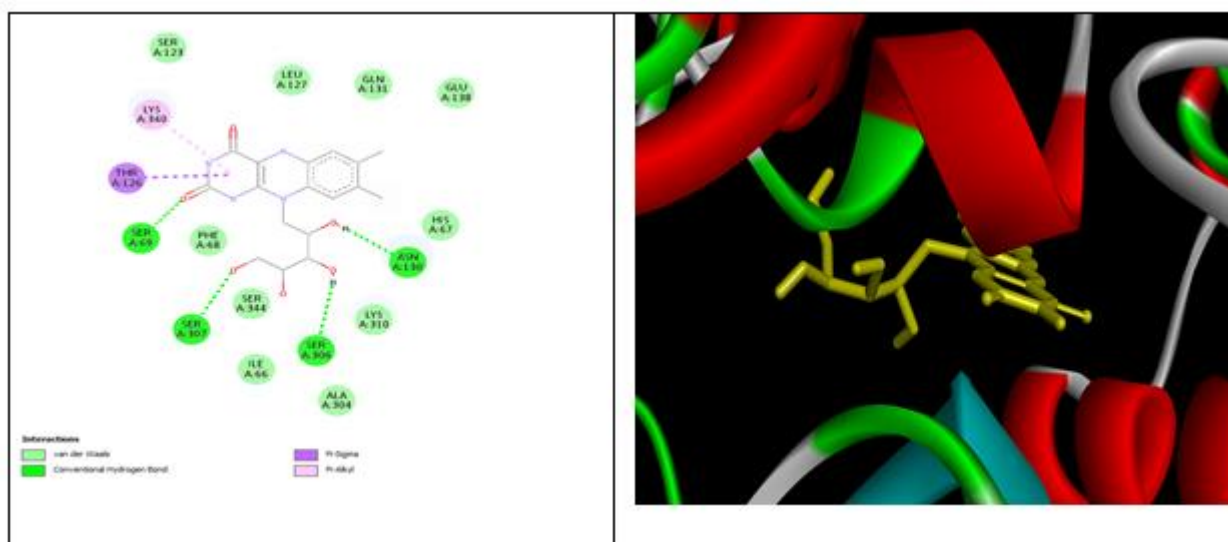


Figure 15: M. 2D and 3D interactions of Thiamine against receptor 1V97.

CONCLUSION

Several polarity phytoconstituents were extracted using a soxhlet device and solvents such as nhexane, chloroform, ethyl acetate, and methanol in order to perform a phytochemical analysis on the leaf powder of *Coccinea grandees*. An occurrence in Saponins, phenols, flavonoids, terpenoids, glycosides, and phytosterol was demonstrated by the methanolic extract. The UV spectra of isolated extract from *Coccinia grandis* was performed using methanol. The UV spectrum showed characteristic bands of fraction in methanol at $\lambda=321,352,413$ The UV spectra of standard showed one characteristic peak at $\lambda=352$. The FTIR analysis of *Coccinia grandis* gave broad peak at 2952.75cm^{-1} which indicated the presence of phenolic O-H stretching. It showed strong peaks at 2921.35cm^{-1} which indicated the presence of alkanes whereas the peaks at 1493.22 and 1378.31cm^{-1} attributed to existence of the aromatic ring's C-C stretching and the C-O stretch, respectively. *In-vitro* anti- nephroprotective like different Concentrations Sample Code CG1 shows low percent of inhibition and against NRK 52E (Kidney Cells) cell line versus a typical medication 5FU. On basis of percent of viability we can conclude that the sample CG1 may not harm the normal kidney cell lines and it may protect the kidney from the harm organ damages. *In-silico* analysis for chemical components of leaf extracts of *C. grandis* was done Using molecular docking, it was revealed how important drug design is for creating new medications that block targets. Most of biomolecules from *C. grandis* leaves were shows better docking results against the active sites of the selected receptor 1V97. Binding energy, hydrogen bond interactions and Vander Waal's interactions for the enzymes are listed in Tables. As the binding energy lowers, binding efficiency will increase. Similarly, as the number of as the number of hydrogen bonds between the ligand and enzyme rises, so does the binding's strength.

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