In-Silico Analysis of Selected Bioactive Compounds Present in Siddha Formulation *Nanthiyavarthathi Pizhi Marunthu* Against *Kan Kasam* (Cataract) Activity

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ABSTRACT

Background

Cataract is one of the leading causes of blindness globally. The enzyme aldose reductase plays a critical role in cataract genesis by catalyzing the reduction of glucose into sorbitol, resulting in osmotic stress and lens epithelial cell apoptosis. Inhibition of this enzyme can delay sorbitol accumulation and prevent or slow cataract development. *Nanthiyavarthathi Pizhi Marunthu*, a Siddha formulation, contains several bioactive phytocomponents with potential aldose reductase inhibitory activity.

Methodology

Ten phytocomponents Voacristine, Lupeol, Moringin, Kaempferol, Rutin, β-sitosterol, Adhatodine, Vasicoline, Anisotine, and Gallic acid were retrieved and subjected to molecular docking against human aldose reductase enzyme (PDB ID: 4GCA) using Auto Dock tools. Epalrestat was used as the standard drug.

Results

All selected phytocomponents exhibited good binding affinity with the active site residues of the aldose reductase enzyme. Rutin (−13.09 kcal/mol; Ki 254.51 pM), β-sitosterol (−12.07 kcal/mol; Ki 1.41 nM), and Anisotine (−10.77 kcal/mol; Ki 12.84 nM) showed the strongest binding energies. The interaction profiles of these compounds were comparable or superior to Epalrestat (−9.90 kcal/mol; Ki 55.17 nM), demonstrating multiple hydrogen bonds with critical amino acid residues.

Conclusion

The molecular docking analysis reveals that the phytocomponents of *Nanthiyavarthathi Pizhi Marunthu* possess strong inhibitory potential against aldose reductase. These compounds may reduce sorbitol accumulation, thereby delaying cataract progression. The findings provide a scientific basis for the traditional use of this Siddha formulation and identify promising lead molecules for further pharmacological and clinical investigations in cataract prevention.

Keywords: Kan kasam, Cataract, *Nanthiyavarthathi Pizhi Marunthu*, Epalrestat

INTRODUCTION

Nanthiyavarthathi Pizhi Marunthu was originally designated to treat foot diseases in the South Indian

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system of medicine called Siddha medicine. In Traditional medicine, *Nanthiyavarthathi Pizhi Marunthu* has been used for the treatment of eyes. Cataracts are a leading cause of cataract blindness globally. The development of cataracts is commonly associated with several different factors, including oxidative stress, oxidative damage to proteins, glycation and inflammatory processes which reduce the clarity and performance of the lens. Although cataract surgery is still the main form of treatment for cataracts, there are very few preventative strategies available for people who will eventually develop cataracts or the means by which to avoid developing cataracts in the first place. There is a need to develop alternative strategies for cataract prevention or treatment [1]. Traditional Siddha medicine offers an extensive variety of formulations made from plants to support health and treat problems that are related to the health of the eyes, including cataract. In South India, the traditional formulation known as *Nanthiyavarthathi Pizhi Marunthu*, which originates from the plant Tabernaemontana divaricata (family Apocynaceae), is widely used as a way of promoting healthy eyes and managing many of the symptoms associated with cataracts. Some studies have shown that this plant contains many bioactive medicinal compounds such as flavonoids, alkaloids, and phenolics that have antioxidant, anti-inflammatory, and protein stabilizing activities [2][3][4]. These compounds act primarily by scavenging harmful free radicals (reactive oxygen species), inhibiting the process of lipid peroxidation, and by preventing the formation of advanced glycation end products through the glycation process. These are the same processes by which cataracts typically develop. In experimental trials using eye lenses from rabbits, researchers have demonstrated that extracts from T. divaricata have the ability to decrease oxidative stress in rabbit lenses, protect and maintain the clarity of rabbit lenses and, most importantly, inhibit the development of cataracts due to glycation-induced aggregation of proteins [5][6]. With the diverse phytochemicals contained in the plant, the evidence that T. divaricata possesses therapeutic benefits, and the documented pharmacological effects of *Nanthiyavarthathi Pizhi Marunthu*, this formulation represents a potential natural intervention to delay or prevent the progression of cataracts. The goal of the present study is to evaluate its protective potential and explore the molecular mechanisms underlying its anti-cataract activity.

LITERATURE REVIEW ON *NANTHIYAVARTHATHI PIZHI MARUNTHU*

Table-1: Ingredients of Nanthiyavarthathi pizhi marunthu

S.No	Botanical Name	Tamil Name	Family
1	*Tabernaemontana divaricate (L.) R.Br. ex Roem & Schult*	Nandiyavattai	Apocynaceae
2	*Moringa oleifera Lam.*	Murungai	Moringaceae
3	*Tribulus terrestris L.*	Nerunjil	Zygophyllaceae
4	*Justicia adhatoda L.*	Adathodai	Acanthaceae
5	*Hygrophylla auriculata Schumach.*	Neer mulli	Acanthaceae

Table 1 lists the six botanical ingredients of *Nanthiyavarthathi Pizhi Marunthu* along with their Tamil names and botanical families. Each plant contributes specific bioactive compounds that support ocular health. Tabernaemontana divaricata is the principal ingredient, known for antioxidant and anti-inflammatory effects [2]. Moringa oleifera and Phyllanthus amarus are rich in flavonoids and phenolics, which help reduce oxidative stress [7][8]. Tribulus terrestris and Eclipta alba possess anti-glycation and protein-protective properties, while Justicia adhatoda contains alkaloids with anti-inflammatory activity [9][10]. Together, these six botanicals provide a synergistic effect, targeting the oxidative, glycation, and inflammatory pathways involved in cataract development [11].

MATERIALS AND METHODS

Molecular Docking

Docking calculations were carried out for retrieved phytocomponents against target Human Aldose reductase enzyme. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of AutoDock tools [12] (*Morris, Goodsell et al., 1998*). Affinity (grid) maps of ×× Å grid points and 0.375 Å spacing were generated using the Autogrid program [12] (*Morris, Goodsell et*

al., 1998). AutoDock parameter set- and distance-dependent dielectric functions were used in the calculation of the van der Waals and the electrostatic terms, respectively. Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method [13] (*Solis and Wets, 1981*). Initial position, orientation, and torsions of the ligand molecules were set randomly. All rotatable torsions were released during docking. Each docking experiment was derived from 2 different runs that were set to terminate after a maximum of 250000 energy evaluations [14]. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied [15].

Phytocomponents selected for Docking:

The list of phytocomponents such as Voacristine, Lupeol, Moringin, Rutin, β-sitosterol, Adhatodine, Vasicoline, Anisotine, Gallic acid which were the components of *Nandhiyavarthathi pizhi marunthu* are selected for docking were listed in Table 2.

ADMET Analysis:

All the canonical structures and SMILES string for evaluation of Absorption, Distribution, Metabolism, Excretion, And Toxicity (ADMET) Characteristics of a compound were obtained from PubChem Database and predicted using tools SwissADME and admet SAR 3.0. It is crucial in understanding a molecule's pharmacokinetics and toxicity. Parameters included Water Solubility, Computed apparent permeability coefficients (Papp) of CaCo2 Permeability across intestinal, MDCK Permeability across tight junctions epithelial cell lines, GI Absorption, Skin permeability, GI Absorption and blood-brain barrier (BBB) permeability [21,22]. Pharmacokinetics of specific drug components in ocular tissues including vitreous is non-uniform. Factors affecting the ADME of a drug molecule in the eye depends on the molecular weight and physicochemical properties such as structure, solubility, logP, stability of the administered drug. Hence these specific parameters were taken into account for ocular bioavailability listed in Table 5 and toxicological parameters especially ocular drug delivery is listed in Table 6 [23,24]

Drug-Likeness Assessment:

Drug-likeness was evaluated based on Lipinski's Rule of Five is tabulated in the Table 4. This rule considers structural properties, including molecular weight (MW), **partition coefficient (Lipophilicity) (Log P)**, hydrogen bond donors (HBD), and hydrogen bond acceptors (HBA), were retrieved from the **above databases listed** in Table 4. It helps to predict and prevent the drug development failures in later stages by choosing the right drug candidates [21,22]

Table – 2: List of Phytocomponents Selected for docking

S.no	Herbs	Phytocomponents	Reference
1	*Tabernaemontana divaricate (L.) R.Br. ex Roem & Schult*	Voacristine,Lupeol, Kaempferol	[16].
2	*Moringa oleifera Lam.*	Moringin	[17]
3	*Tribulus terrestris L.*	Rutin, β-sitosterol	[18]
4	*Justicia adhatoda L.*	Adhatodine , Vasicoline, Anisotine	[19]
5	*Hygrophylla auriculata Schumach.*	Gallic acid	[20]

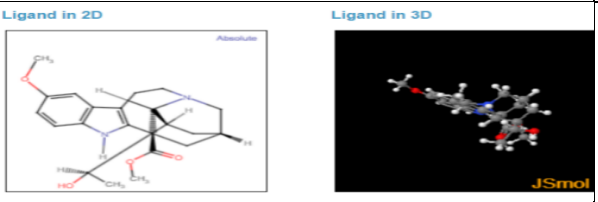
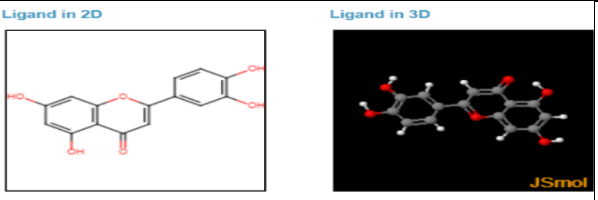
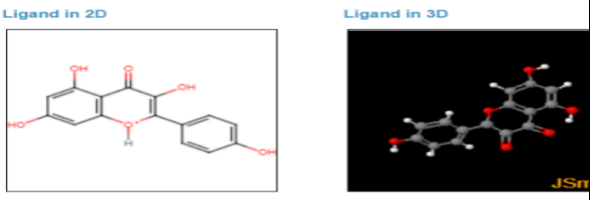
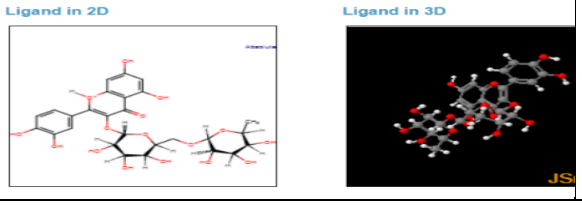
3D- Structure of Human Aldose reductase enzyme (PDB) - 4GCA

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RECEPTOR STRUCTURE

Table-3. 2D and 3D structure of Phytocomponents of *nanthiyavarthathi pizhi marunthu*

Phyto components	Mol Formula	2D and 3D structure	PubChem (CID)
Voacristine	$C_{14}H_{17}NO_5S$		44566752
Lupeol	$C_{30}H_{50}O$		259846
Moringin	$C_{14}H_{17}NO_5S$		153557
Kaempferol	$C_{15}H_{10}O_6$		5280863
Rutin	$C_{27}H_{30}O_{16}$		5280805

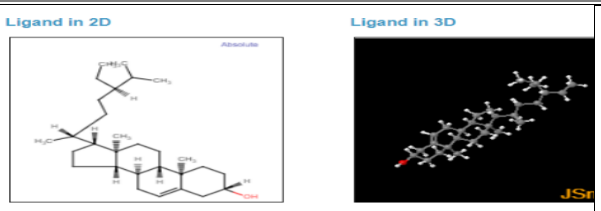
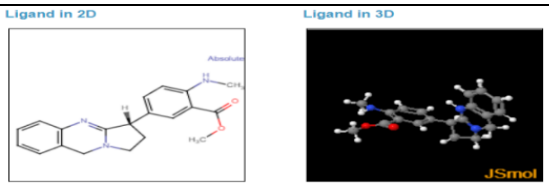
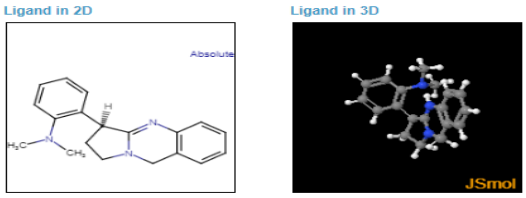
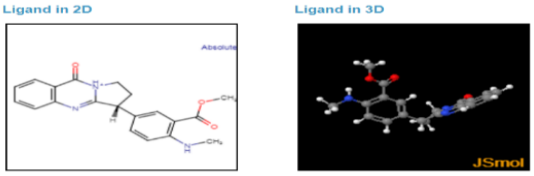
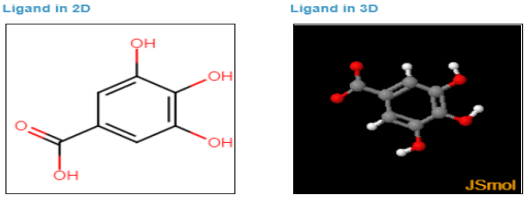
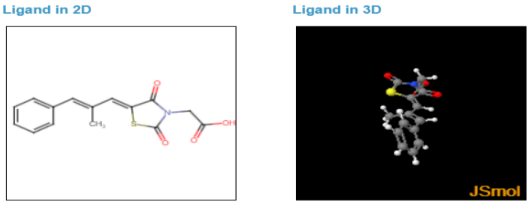
β-sitosterol	$C_{29}H_{50}O$		222284
Adhatodine	$C_{20}H_{21}N_3O_2$		5316460
Vasicoline	$C_{19}H_{21}N_3$		626005
Anisotine	$C_{20}H_{19}N_3O_3$		442884
Gallic acid	$C_7H_6O_5$		370
Epalrestat	$C_{15}H_{13}NO_3S_2$		1549120

Table-4 Molecular data from PubChem following Lipinski's Rule.

Compound	Molar weight g/mol	Consensus Log P	H Bond Donor	H Bond Acceptor	Rotatable bonds	No. of Violations
Voacristine	384.5 g/mol	1.81	2	5	4	0
Lupeol	426.7g/mol	7.33	1	1	1	1
Moringin	311.36 g/mol	1.41	3	6	4	0
Kaempferol	286.24 g/mol	1.3	4	6	1	0
Rutin	610.5 g/mol	-1.78	10	16	6	3
β-sitosterol	414.7g/mol	7.37	1	1	6	1
Adhatodine	335.416 g/mol	3.06	1	3	4	0
Vasicoline	291.4 g/mol	3.19	0	1	2	0
Anisotine	349.4 g/mol	2.63	1	4	4	0
Gallic acid	170.12 g/mol	0.26	4	5	1	0
Epalrestat	319.4 g/mol	2.72	1	3	4	0

Table 5: ADME properties of Selected Compounds

Compounds	TPSA (Å²)	ESOL Class	Caco-2 P_{app}(x 10^6 cm/s)	MDCK P_{app}(x 10^6 cm/s)	GI absorption	BBB permeant	P-gp Substrate	Log Kp (cm/s) (Skin Permeability)
Voacristine	74.79	Soluble	1.75	6.62	High	Yes	Yes	-6.97
Lupeol	20.23	Poorly soluble	6.19	10.4	Low	No	No	-1.9
Moringin	123.6	Soluble	2.7	12.8	High	No	No	-7.27
Kaempferol	111.13	Soluble	1.07	12.3	High	No	No	-6.67
Rutin	269.43	Soluble	0.284	9.4	Low	No	Yes	-11.34
β-Sitosterol	20.23	Poorly soluble	7.54	11.6	Low	No	No	-2.2
Adhatodine	53.93	Soluble	4.02	14	High	Yes	Yes	-6.16
Vasicoline	18.84	Soluble	31.4	21.6	High	Yes	Yes	-6.08
Anisotine	73.22	Moderately soluble	4.62	14.7	High	Yes	No	-5.31
Gallic acid	97.99	Very soluble	2.49	15.6	High	No	No	-6.84
Epalrestat	115	Moderately soluble	4.28	11	High	No	No	-5.52

Metrics expressed as linear velocities scaled to × 10^{-6} cm/s and rounded to three significant figures.

Table 6: Toxicity parameters of Selected Compounds

Compounds	Rodents Carcinogenicity	Eye corrosion	Eye irritation	Ames mutagenesis
Voacristine	0.457	0.002	0.001	0.507
Lupeol	0.349	0.772	0.848	0.118
Moringin	0.748	0.112	0.251	0.784
Voacristine	0.457	0.002	0.001	0.507
Lupeol	0.349	0.772	0.848	0.118
Moringin	0.748	0.112	0.251	0.784
Kaempferol	0.805	0.959	0.27	0.725
Rutin	0.473	0.019	0.27	0.515
β-Sitosterol	0.322	0.698	0.823	0.118
Adhatodine	0.591	0.028	0.264	0.51
Vasicoline	0.453	0.041	0.109	0.363
Anisotine	0.643	0.001	0.014	0.658
Gallic acid	0.524	0.497	0.979	0.331
Epalrestat	0.606	0.026	0.172	0.586

Table – 6: Summary of the molecular docking studies of compounds against Human Aldose reductase enzyme (PDB) - 4GCA

Compound	Est. Free Energy of Binding	Est. Inhibition Constant, Ki	Electrostatic Energy	Total Intermolec. Energy	Interact. Surface
Voacristine	-8.82 kcal/mol	343.76 nM	-0.11 kcal/mol	-9.26 kcal/mol	845.362
Lupeol	-10.06 kcal/mol	41.97 nM	-0.01 kcal/mol	-10.80 kcal/mol	874.269
Moringin	-4.87 kcal/mol	268.71 uM	-0.51 kcal/mol	-5.52 kcal/mol	357.69

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Kaempferol	-7.24 kcal/mol	4.90 uM	-0.02 kcal/mol	-7.60 kcal/mol	721.014
Rutin	-13.09 kcal/mol	254.51 pM	-0.01 kcal/mol	-8.84 kcal/mol	970.051
β-sitosterol	-12.07 kcal/mol	1.41 nM	-0.03 kcal/mol	-13.91 kcal/mol	908.069
Adhatodine	-9.30 kcal/mol	151.93 nM	-0.00 kcal/mol	-9.90 kcal/mol	870.015
Vasicoline	-9.83 kcal/mol	61.98 nM	-0.06 kcal/mol	-9.73 kcal/mol	723.939

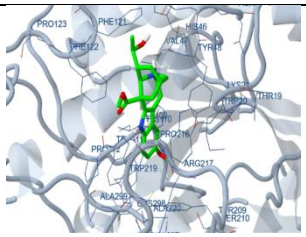
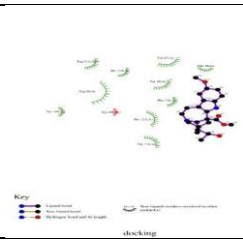
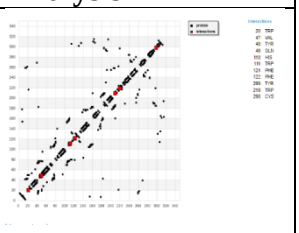
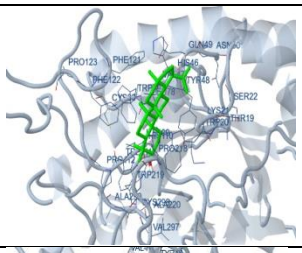
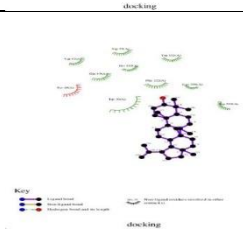
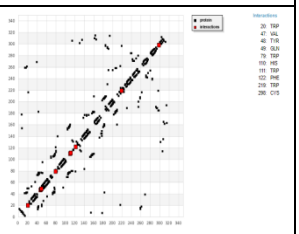
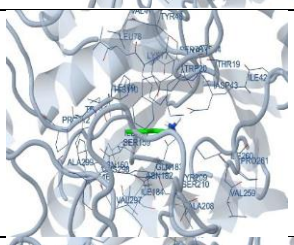
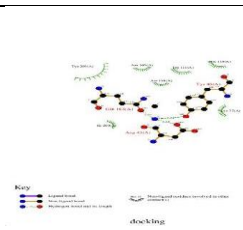
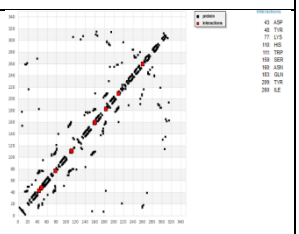
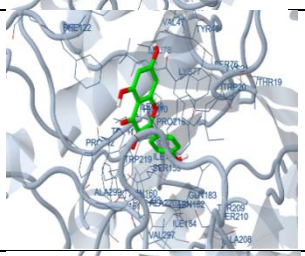
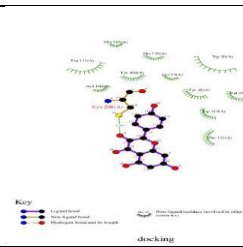
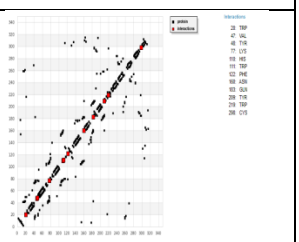
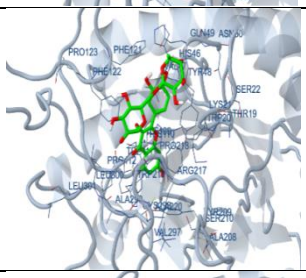
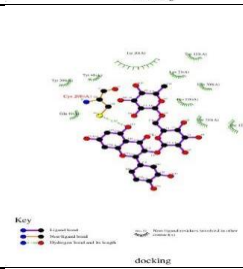
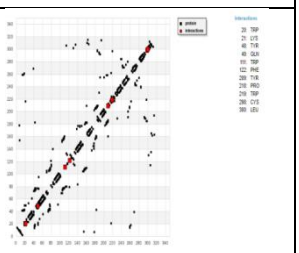
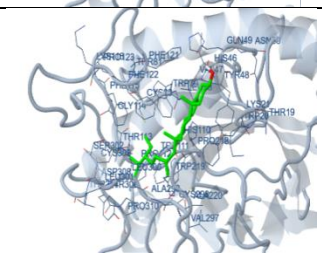
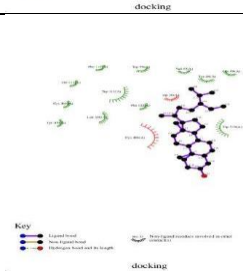
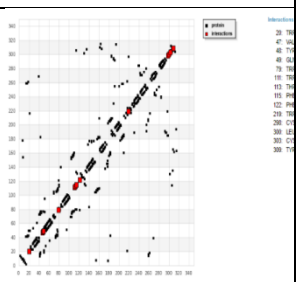
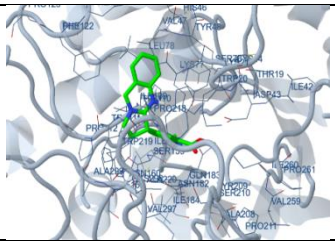
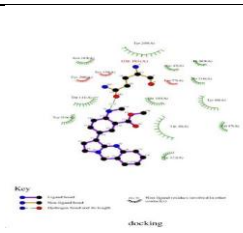
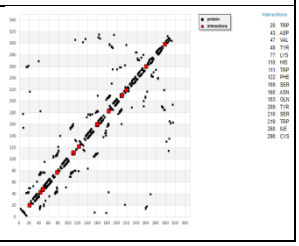
Anisotine	-10.77 kcal/mol	12.84 nM	-0.10 kcal/mol	-11.34 kcal/mol	884.125
Gallic acid	-5.80 kcal/mol	55.80 uM	-1.10 kcal/mol	-5.32 kcal/mol	430.62
Epalrestat	-9.90 kcal/mol	55.17 nM	-0.85 kcal/mol	-11.24 kcal/mol	725.143

Table 7: Amino acid Residue Interaction of Lead against Human Aldose reductase enzyme (PDB) - 4GCA

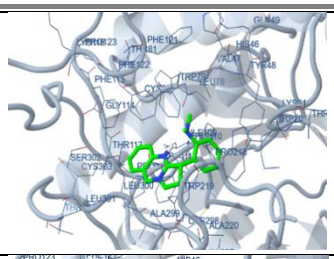
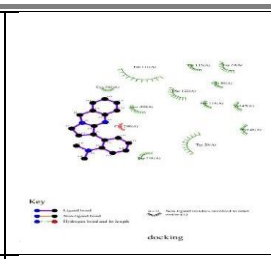
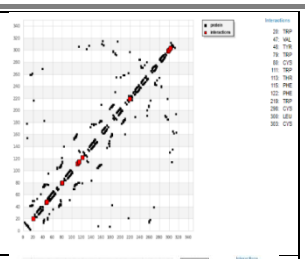
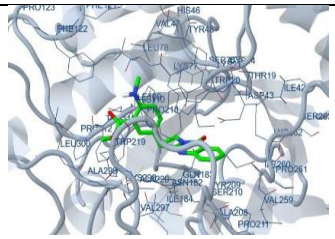
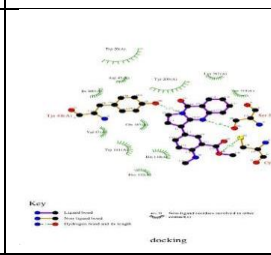
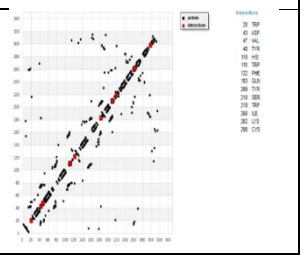
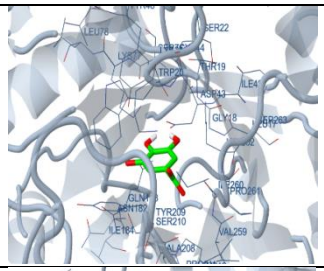
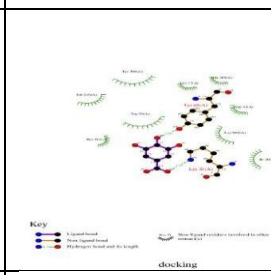
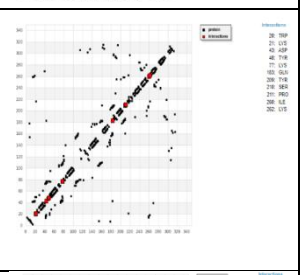
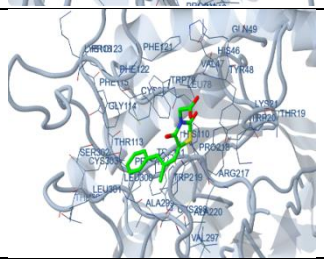
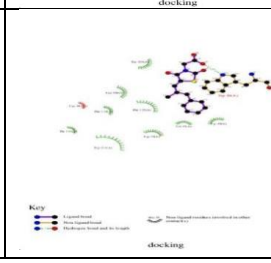
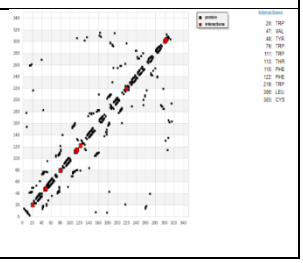
Compound	**Interactions**	**Amino acid Residues**															
Voacristine	7	20	47	48	49	110	111	121	122	209	219	298					
		TRP	VAL	TYR	GLN	HIS	TRP	PHE	PHE	TYR	TRP	CYS					
Lupeol	8	20	47	48	49	79	110	111	122	219	298						
		TRP	VAL	TYR	GLN	TRP	HIS	TRP	PHE	TRP	CYS						
Moringin	5	43	48	77	110	111	159	160	183	209	260						
		ASP	TYR	LYS	HIS	TRP	SER	ASN	GLN	TYR	ILE						
Kaempferol	8	20	47	48	77	110	111	122	160	183	209	219	298				
		TRP	VAL	TYR	LYS	HIS	TRP	PHE	ASN	GLN	TYR	TRP	CYS				
Rutin	6	20	21	48	49	111	122	209	218	219	298	300					
		TRP	LYS	TYR	GLN	TRP	PHE	TYR	PRO	TRP	CYS	LEU					
β-sitosterol	8	20	47	48	49	79	111	113	115	122	219	298	300	303	309		
		TRP	VAL	TYR	GLN	TRP	TRP	THR	PHE	PHE	TRP	CYS	LEU	CYS	TYR		
Adhatodine	7	20	43	47	48	77	110	111	122	159	160	183	209	210	219	260	298
		TRP	ASP	VAL	TYR	LYS	HIS	TRP	PHE	SER	ASN	GLN	TYR	SER	TRP	ILE	CYS
Vasicoline	8	20	47	48	79	80	111	113	115	122	219	298	300	303			
		TRP	VAL	TYR	TRP	CYS	TRP	THR	PHE	PHE	TRP	CYS	LEU	CYS			
Anisotine	8	20	43	47	48	110	111	122	183	209	210	219	260	262	298		
		TRP	ASP	VAL	TYR	HIS	TRP	PHE	GLN	TYR	SER	TRP	ILE	LYS	CYS		
Gallic acid	4	20	21	43	48	77	183	209	210	211	260	262					
		TRP	LYS	ASP	TYR	LYS	GLN	TYR	SER	PRO	ILE	LYS					
Epalrestat	8	20 TRP	47 VAL	48 TYR	79 TRP	111 TRP	113 THR	115 PHE	122 PHE	219 TRP	300 LEU	303 CYS					

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Table- 8: ***Docking Pose of compounds with Human Aldose reductase enzyme (PDB) - 4GCA***

phytochemical	**Docking pose with *Human Aldose reductase enzyme (PDB) - 4GCA***	**2D interaction plot analysis**	**Hydrogen bond plotting with core amino acid Analysis**
Voacristine			
Lupeol			
Moringin			
Kaempferol			
Rutin			
β-sitosterol			
Adhatodine			

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Vasicoline			
Anisotine			
Gallic acid			
Epalrestat			

Observation and Inference

Total of 10 bioactive lead compounds were retrieved from the herbs present in the siddha formulation listed in Table 2. It was observed from the present investigation that the phytochemicals such as Voacristine, Lupeol, Moringin, Kaempferol, Rutin, β-sitosterol, Adhatodine, Vasicoline and Anisotine reveals maximum of 5 to 8 viable interactions with the residual amino acid present in the target aldose reductase enzyme when compared to that of the stands Epalrestat which impose 8 viable interactions with residual amino acid of the target enzyme.

DISCUSSION

The initial screening of Lipinski criteria revealed that eight out of the eleven compounds (Voacristine, Moringin, Kaempferol, Adhatodine, Vasicoline, Anisotine, Gallic acid, and Epalrestat) demonstrated zero violations against Lipinski's parameters. These compounds possess low-to-moderate consensus lipophilicity profiles, enabling them to satisfy baseline drug-likeness criteria. Conversely, Lupeol and β-Sitosterol exhibited a single violation driven exclusively by extreme lipophilicity thresholds; their elevated Log P values indicate an excessively hydrophobic core. The most divergent compound across these rules was Rutin, which logged three independent violations. Rutin exceeded the standard molecular size restriction while demonstrating a highly hydrophilic profile, suggesting it may not be able to cross tight biological membranes via passive diffusion, especially across corneal tight junctions. While Rutin may possess favorable downstream antioxidant properties, nanocarrier-based formulations should be investigated as a potential strategy to improve its delivery, subject to further experimental validation.

Regarding predictive toxicity profiles, Vasicoline emerged as the most promising lead, combining high Caco-2/MDCK permeability with an exceptional local safety profile (tracking as both non-irritant and non-corrosive). Conversely, while highly lipophilic candidates like Lupeol and β-sitosterol offer robust

membrane affinity, their severe water insolubility and elevated eye-irritation alerts mandate the use of advanced nano-carrier formulation strategies to achieve safe, effective ocular delivery.

The molecular docking analysis shows that several phytocompounds can strongly inhibit the target protein. Many candidates have better affinity than the standard drug, Epalrestat. The docking scores suggest that compounds with complex polyphenolic or sterol-based structures have higher binding affinity. This is because they can form multiple stabilizing interactions within the active site. This finding is consistent with research in Indian pharmacognosy and phytochemistry, which often identifies flavonoids and phytosterols as effective modifiers of enzyme activity [26][27][28].

The docking study binding energy table compares several compounds against a standard, Epalrestat, to evaluate their binding affinities and related docking parameters. Binding energy (estimated free energy of binding) is a crucial parameter, where a lower (more negative) value suggests stronger binding to the target protein. Epalrestat serves as a reference compound due to its already established pharmacological activity. Epalrestat, the control compound, shows a binding energy of -9.90 kcal/mol, an inhibition constant (Ki) of 55.17 nM, and total intermolecular energy of -11.24 kcal/mol. The tested phytocompounds such as Lupeol: -10.06 kcal/mol, similar free energy but better Ki (41.97 nM). Anisotine: -10.77 kcal/mol, Ki 12.84 nM, had notable binding. Phytocompounds such as Moringin: -4.87 kcal/mol, Ki 268.71 μM, Kaempferol: -7.24 kcal/mol, Ki 4.90 μM. Gallic acid: -5.80 kcal/mol, Ki 55.80 μM. shows weak binding and are less potent compared to Epalrestat. Compounds like Rutin and β-sitosterol, with much lower (more negative) binding energies and lower Ki values, show stronger predicted binding than Epalrestat and could offer higher potency.

Compounds with higher (less negative) binding energy, such as Moringin and Gallic acid, are less likely to be effective inhibitors compared to the control. Epalrestat's performance is solid, but the discovery of certain phyto-compounds with stronger binding in silico underlines their potential for further in vitro and in vivo evaluation as alternatives or adjunctive agents.Total intermolecular energy and electrostatic contributions also influence binding, with β-sitosterol showing particularly favorable values (-13.91 kcal/mol) versus Epalrestat (-11.24 kcal/mol).Interaction surface area is largest for Rutin (970.051), indicating a possibly larger contact footprint on the target protein, which may contribute to improved binding.

Rutin, a flavonoid glycoside included in this study, is a large compound that exhibits high affinity toward protein ligands. This suggests that bulky molecules with extensive hydrogen-bonding capabilities can stabilize the ligand–receptor complex through a combination of hydrophobic and hydrophilic interactions. Previous studies on Rutin's docking affinity toward inflammatory and metabolic targets further emphasize its medicinal relevance in various diseases [29][30]. The study results can be justified by the reports from previous research works that treatment with rutin prevented the loss of α crystallin chaperone property, and protein insolubilization prevailed during selenite-induced cataract [31].

Phytosterols, particularly β-sitosterol, also showed robust binding characteristics, consistent with earlier Indian studies demonstrating that sterol frameworks readily integrate into hydrophobic pockets of target enzymes [32][33]. Such strong interactions may translate to meaningful biological activity, as β-sitosterol is known to exert anti-inflammatory, antioxidant effects, which complement the predicted inhibitory mechanism observed in this study'.

Activation of the polyol pathway (via aldose reductase), osmotic stress, electrolyte imbalance, and protein insolubilization are reported to be associated with Cataract formation. β-Sitosterol–containing extracts have been shown to inhibit aldose reductase activity, reduce sorbitol accumulation, and help normalize lens Na^+/K^+ levels, thereby protecting lens transparency [34]. The presence of phytocompound β-sitosterol in this study drug can be regarded as a key phytoconstituent responsible for these effects as studies report that extracts rich in β-sitosterol reduced selenite- or glucose-induced lens opacity, preserved lens protein content, and lowered markers of oxidative damage, implicating. A similar in vitro lens study on plant extracts with β-sitosterol reported protection against oxidative stress–induced opacification, including better maintenance of lens electrolyte balance and protein levels [35,36].

Alkaloids from *Justicia adhatoda*, such as Anisotine, also displayed high affinity, reinforcing traditional Siddha and Ayurvedic reports that highlight their pharmacological potency. Their docking performance, supported by literature on bronchodilatory and anti-inflammatory actions, suggests that these compounds may interact with enzyme catalytic residues through both hydrophobic and π–π stacking interactions [37][10]. This makes them strong candidates for further biological evaluation. Though there are not much studies on the direct action of Anisotine on cataract endpoints, general cataract reviews emphasize that herbal preparations rich in antioxidants can delay or reduce lens opacity by scavenging reactive oxygen species, preventing protein aggregation, and protecting lens epithelium [38].

Compounds with weaker binding affinities in this study largely belong to smaller phenolic structures. Their limited interaction profiles indicate that molecular size and chemical complexity play critical roles in determining docking success. This trend is consistent with several Indian reports on flavonoid–enzyme interactions, where smaller phenolics show modest inhibition compared with larger glycosylated derivatives [39].

Overall, the docking outcomes indicate that Rutin, β-sitosterol, and Anisotine emerge as promising lead molecules, outperforming the standard drug and showing characteristics consistent with previous in vitro and in silico reports from Indian medicinal plant research. The results justify prioritizing these compounds for in vitro enzyme inhibition assays, cell-based anti-inflammatory evaluations, and in vivo validation, especially considering their established safety in traditional medicine systems. The convergence of docking evidence and ethnomedicinal relevance underscores the potential of these phytochemicals as future therapeutic candidates or adjuncts.

CONCLUSION

Based on the results of the computational analysis it was concluded that the bio-active compound's like Rutin, β-sitosterol, and Anisotine emerge as promising lead molecules, present in the herbal ingredients of *Nanthiyavarthathi Pizhi Marunthu* possess significant binding affinity against the target aldose reductase enzyme by interacting with active amino acid present on the active site. Thereby it was concluded that these phytocomponents that selectively inhibit the function of the enzyme aldose reductase that would result in delay sorbitol accumulation and subsequent cataract development.

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