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Original Research Article

Psoriasis Vrs Cassia Fistula: In-Silico Study

Mr. Chandra Sekhar Tripathy[1], Dr. Anil Kumar[2], Prof. Ghassem Habibi Bibalani[3], Dr. Santosh Kumar Behera[4], Santanu Kumar Budhia[5], Dr. P K Mohanta[6], Easter Khura[7], Dr. Asadollah Asadi[8], Dr. Arash Abdolmaleki[9], Prof. Muhammad Akram[10], Dr. Debasish Mishra[11], Deepak Bhattacharya[12*]

[1]M. Sc., Regional Medical Research Centre, Bhubaneswar, Odisha, India,
[2]Principal Scientist & Head, Division of Design of Experiments I.C.A.R-I.A.S.R.I., Library Avenue, New Delhi, India, PIN- 110012
[3]Ph.D, Department of Natural Resources, Shabestar Branch, Islamic Azad University, Shabestar, Iran
[4]Ph.D., Scientist Grade II, National Institute of Pharmaceutical Education and Research, Ahmedabad, Gujarat, India
[5]BA; Traditional Ayurvedacharya, Nagharen Temple Rd, Baabajee Padaa, Balangir, Odisha, India
[6]MD (Ay), Govt Drug Inspector; Registrar Ay Council; Principal, IGMMC & amp; Hospital, H-2/58, SS Enclave, Khandagiri, Bhubaneswar-751030, Odisha, India
[7]M Sc (nursing), Vice Principal, School of Nursing, Raxaul, Bihar, India – 845305
[8]Associate Professor, Department of Biology, University of Mohaghegh Ardabili, Iran
[9]Assistant Professor, Animal Physiology, University of Mohaghegh Ardabili, Faculty of Advanced Technologies, Department of Biology, Ardabil Province, Ardabil, Daneshgah St, Iran
[10]BEMS, M.Phil, Ph.D, Chairperson, Dept. of Eastern Medicine, Government Collage University, Faisalabad, Pakistan
[11]MBBS, Director – Govt Blood Bank – Apex, Capital Hospital, Bhubaneswar, Odisa, India – 751009
[12]Ph.D., Policy, Nursing, At Fight-Cancer at Home, Medicinal Toxicology & QC, At : Sri Radha Krishna RaasMandir, KedarGouri Road, Bhubaneswar–751002,Odisa, India.

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***Corresponding Author:** Deepak Bhattacharya, Ph.D
Policy, Nursing, At Fight-Cancer at Home, Medicinal Toxicology & QC, At : Sri Radha Krishna RaasMandir, Kedar Gouri Road, Bhubaneswar–751002,Odisa, India.
Email: fightcancermetastasisathome@gmail.com

Abstract

Psoriasis is a skin disease. It is rare growing disease around the world. Here in this investigation we have targeted a protein namely TRPV3 (Transient receptor potential cation channel, subfamily III) ion channel for the study of psoriasis, which is important factor of psoriasis. The medicinal plant namely Cassia fistula is selected for the in silico investigation. 39 phyto compounds as reported in various research papers are taken for study. Out of 39 phytochemicals, Chrysophanol compound showed highest binding affinity of -7.58kcal/mol having 3 conventional Hydrogen bonds with TRPV3 protein and is found to be a better natural compound as compared to other reported drugs generally used to for the psoriasis. This investigation will lead to more and better findings leading to drug discovery & use as functional food.

Keywords: Psoriasis; TRPV3 ion channel; Cassia fistula; Molecular docking; in silico study.

INTRODUCTION

Skin is the largest organ. And the one that also is connected to the (i) vital physiological process (ii) deep brain (iii) entire neuronal circuit (iv) experiences maximum weathering 24 x 7. Psoriasis and its variants are a chronic immune-mediated inflammatory malady of the skin. Initial variant can change during malady in-situ period with or without a nexus to small bone joints & tendons viz., psoriatic arthritis (metabolic pathways). Is acutely debilitating; disconcerting and inflicts deep psychological stress 24 x 7. It can happen to anyone, anytime. Are non-communicable; not vectorable; yet chance filial. Thus far every variant have failed curative efforts- century scale [R-1]. Various genes and systemic factors are involved. Phyto; hormone; aroma; cholinergic; carcinogens; anti-tissue; anti-neoplastic (solid & liquid tumors\cancers); target; monoclonal

anti-body; target; repurposed; etc., therapies (every school) have all been tried with non yielding any (even near assured) drug dose repeatable results. Too many have indicated unacceptable contradictions and individual specific biphasic character post initial few dose of positive indication. Non leave identical traces of metabolic; drug mechanics and kinematics (unacceptable). Animal models are unethical and moreover have proved as idiotic. This has posited psoriasis as an enigma and its clinical management as pharmacist's & physician's dilemma. There is no therapy [R-2]. Due such historical track of failure in anti-psoriasis drug discovery it has become very expensive; frown-full with disapprovals from the support frame work. Thus there is a need for a paradigm shift in (neo) drug source\starting material i.e., pre-screening viz., in-silico study. We have selected the economic and abundant Cassia fistula belonging to kingdom plantae, family Fabacae, genus Cassia and spp., Fistula [R-3]; it is more known as an ornamental\ promenade tree. In Ayurveda this genus is described to be useful in skin diseases, cardiac disorders, tuberculosis, liver, leukemia; diabetes; constipation related problems and in mono and poly herbal modern formulations. It is abundantly available in the entire tropo-equatorial belts worldwide. However, it has not been used in the caption domain pre to this communication. Here we report the docking specificity of its natural compounds with the principal (anthropogenic) gene that is responsible for the malady psoriasis. This is an original; 1st time and yet is only an indicative work as assistance to others.

MATERIALS& METHODS

Gene selection for the study

The gene 'Transient receptor potential cation channel, subfamily III' (TRPV-3) has been selected as it is the most involvedin thepatho-physiology of all psoriasis variants & stages [R-4].

Phyto-Sources

Herbs are veritable source for drug discovery. There are a many different types of medicinal plants in nature which all on psoriasis have varying effect between them with non-reproducing therapeutic efficacy. They also fall acutely short of efficacy as compared to conventional drugs. While such conventional treatments have remained limited to steroids cum toxic moieties; carcinogens; functional food and changes in life style. Herbal combinations thus far have also not provide any panacea. Moreover, all natural sources necessarily are not nontoxic. Nontoxic therapy is the call of present times. Therefore, there is a crying need & opportunity. In this communication we have selected (almost all) the known natural compounds of the tree*Cassia fistula Linn.* Fabaceace(Fig-1 (a) and (b)). It is non-toxic [Ref -5]; not noted in Classical Ayurveda [R-6, 7]; nor in Sino schools [R-8]. However, *Cassia angustifolia*Vahl is mentioned in the Ayurvedic Pharmacopeia & in the official formularies, respectively [R-9; 10]. Whereas, post independent Indian Scientific Compendiums of medicinal plants of india deals with *fistula* abundantly [R-11, 12 and 13]. None of the works indicate any usage vis-à-vis Psoriasis.

Fig-1(a): Shows Cassia Fistula the summer flowering tree with fruits as on 1-11-2021., Bhubaneswar, India and (b) shows the bark on its trunk. It contains Chrysophanol the most sans Oxyanthraquinone.

PHYTOCHMICALS OF Cassia fistula

Cassia fistula has 39 phyto-chemicals (PC) with accepted structures in thePubChem database[R-14]. Table-1 enumerates the details. These were verified and matched [R-15, 16, 17 and 18].

Ro5 and Toxicity Studies

Plants contain divergent compounds including toxins & toxicity up-regulators. Medicinal plants (as a rule) contain the least & normally the most unstable\auto degrading toxins, hence = medicinal.

Psoriasis also responds\becomes unstable transiently to sub-clinical doses of (nearly all) toxins. Finally rebounds. We are interested in a non-toxic route of therapeutics (pregnancy safe). Therefore, toxicity evaluation is priority.

Hence, Lipinski's Rule of Five (RO5) study was carried out using TargetNet web server (standard tool for such purposes) and 17 out of the 39 (43.58%) phyto compounds (PC) satisfied all the rules (Table 2). The 17 PCs which qualified the RO5 test were again studied via ProTox-II server to check their Toxicity (https://mcule.com/apps/toxicity-checker/)[R-19](https://tox-new.charite.de/protoxII/).

RESULTS (TOXICITY)

Out of the 17 PCs, 16 (94.12%) are found to be Non-Toxic (Table 3). These 16 PCs were finally taken for the docking study against TRPV3 protein.

Table-1: Description of Phytochemical compounds present in *Cassia fistula*

SL. No.	Chemical name	Molecular formula	PMID	SMILE ID
1.	Cyclopentasiloxane, Decamethyl	$C_{10}H_{30}O_5Si_5$	10913	C[Si]1(O[Si](O[Si](O[Si](O[Si](O1)(C)C)(C)C)(C)C)(C)C)(C)C
2.	Cyclohexasiloxane, dodecamethyl	$C_{12}H_{36}O_6Si_6$	10911	C[Si]1(O[Si](O[Si](O[Si](O[Si](O[Si](O1)(C)C)(C)C)(C)C)(C)C)(C)C)(C)C
3.	Citronellol	$C_{10}H_{20}O$	8842	CC(CCC=C(C)C)CCO
4.	Isophytol	$C_{20}H_{40}O$	10453	CC(C)CCCC(C)CCCC(C)CCCC(C)(C=C)O
5.	1,3-Cyclopentadiene, 5-(1-methylethylidene)-	C_8H_{10}	137467	CC(=C1C=CC=C1)C
6.	Phytol	$C_{20}H_{40}O$	5280435	CC(C)CCCC(C)CCCC(C)CCCC(=CCO)C
7.	Pyridine	C_5H_5N	1049	C1=CC=NC=C1
8.	Linolenic acid	$C_{18}H_{30}O_2$	5280934	CCC=CCC=CCC=CCCCCCCCC(=O)O
9.	Oxyanthraquinone	$C_{14}H_9NO_3$	8323	C1=CC=C2C(=C1)C(=O)C3=C(C=CC(=C3C2=O)O)N
10.	dihydroxyanthraquinone	$C_{22}H_{28}N_4O_6$	4212	C1=CC(=C2C(=C1NCCNCCO)C(=O)C3=C(C=CC(=C3C2=O)O)O)NCCNCCO
11.	epiafzelechin	$C_{15}H_{14}O_5$	443639	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC=C(C=C3)O)O
12.	epicatechin	$C_{15}H_{14}O_6$	72276	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O
13.	procyanidin B2	$C_{30}H_{26}O_{12}$	122738	C1C(C(OC2=C1C(=CC(=C2C3C(C(OC4=CC(=CC(=C34)O)O)C5=CC(=C(C=C5)O)O)O)O)O)C6=CC(=C(C=C6)O)O)O
14.	rhein	$C_{15}H_8O_6$	10168	C1=CC2=C(C(=C1)O)C(=O)C3=C(C2=O)C=C(C=C3O)C(=O)O
15.	rhein glucoside	$C_{21}H_{18}O_{11}$	5320961	C1=CC2=C(C(=C1)OC3C(C(C(C(O3)CO)O)O)O)C(=O)C4=C(C2=O)C=C(C=C4O)C(=O)O
16.	sennoside A	$C_{42}H_{38}O_{20}$	73111	C1=CC2=C(C(=C1)OC3C(C(C(C(O3)CO)O)O)O)C(=O)C4=C(C2C5C6=C(C(=CC=C6)OC7C(C(C(C(O7)CO)O)O)O)C(=O)C8=C5C=C(C=C8O)C(=O)O)C=C(C=C4O)C(=O)O
17.	sennoside B	$C_{42}H_{38}O_{20}$	91440	C1=CC2=C(C(=C1)OC3C(C(C(C(O3)CO)O)O)O)C(=O)C4=C(C2C5C6=C(C(=CC=C6)OC7C(C(C(C(O7)CO)O)O)O)C(=O)C8=C5C=C(C=C8O)C(=O)O)C=C(C=C4O)C(=O)O
18.	chrysophanol	$C_{15}H_{10}O_4$	10208	CC1=CC2=C(C(=C1)O)C(=O)C3=C(C2=O)C=CC=C3O
19.	physcion	$C_{16}H_{12}O_5$	10639	CC1=CC2=C(C(=C1)O)C(=O)C3=C(C2=O)C=C(C=C3O)OC
20.	Kaempferol	$C_{15}H_{10}O_6$	5280863	C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O
21.	leucopelargonidin tetramer	$C_{60}H_{50}O_{16}$	102115508	C1CC2=C(C(=C(C=C2O)O)C3CC(OC4=C3C(=CC(=C4C5CC(OC6=C(C(=CC(=C56)O)O)O)C7CC(OC8=CC(=CC(=C78)O)O)C9=CC=C(C=C9)O)C2=CC=C(C=C2)O)O)O)C2=CC=C(C=C2)O)OC1C1=CC=C(C=C1)O
22.	Fistulic acid	$C_{18}H_{14}O_8$	53438729	CC1=C(C(=C2C(=C1O)C(=O)C3=CC(=C(C=C3C2=O)OC)OC)O)C(=O)O
23.	Proanthocyanidins	$C_{30}H_{26}O_{13}$	122173182	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)OC4(C(C(C5=C(C=C(C=C5O4)O)O)O)O)C6=CC(=C(C=C6)O)O
24.	Catechin	$C_{15}H_{14}O_6$	9064	C1C(C(OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O
25.	Diethyl Phthalate	$C_{12}H_{14}O_4$	6781	CCOC(=O)C1=CC=CC=C1C(=O)OCC
26.	Cyanoacetylurea	$C_4H_5N_3O_2$	74055	C(C#N)C(=O)NC(=O)N
27.	o-Veratramide	$C_9H_{11}NO_3$	220089	COC1=CC=CC(=C1OC)C(=O)N
28.	1,5-Diphenyl-2H-1, 2, 4-triazoline -3-thione	$C_{14}H_{11}N_3S$	2802516	C1=CC=C(C=C1)C2=NC(=S)NN2C3=CC=CC=C3
29.	Sarcosine	$C_3H_7NO_2$	1088	CNCC(=O)O
30.	Patuletin	$C_{16}H_{12}O_8$	5281678	COC1=C(C2=C(C=C1O)OC(=C(C2=O)O)C3=CC(=C(C=C3)O)O)O
31.	Methyl succinic acid	$C_5H_8O_4$	10349	CC(CC(=O)O)C(=O)O
32.	Menisdaurin	$C_{14}H_{19}NO_7$	6440400	C1C(C=CC(=CC#N)C1OC2C(C(C(C(O2)CO)O)O)O)O
33.	Robustaflavone	$C_{30}H_{18}O_{10}$	5281694	C1=CC(=CC=C1C2=CC(=O)C3=C(O2)C=C(C(=C3O)C4=C(C=CC(=C4)C5=CC(=O)C6=C(C=C(C=C6O5)O)O)O)O)O
34.	1-Galloyl-Beta-D-glucose	$C_{13}H_{16}O_{10}$	124021	C1=C(C=C(C(=C1O)O)O)C(=O)OC2C(C(C(C(O2)CO)O)O)O
35.	Hydroxysafflor yellow A	$C_{27}H_{32}O_{16}$	6443665	C1=CC(=CC=C1C=CC(=C2C(=C(C(=O)C(C2=O)(C3C(C(C(C(O3)CO)O)O)O)O)C4C(C(C(C(O4)CO)O)O)O)O)O)O
36.	Undulatoside A	$C_{16}H_{18}O_9$	5321494	CC1=CC(=O)C2=C(C=C(C=C2O1)OC3C(C(C(C(O3)CO)O)O)O)O
37.	Procyanidin B2	$C_{30}H_{26}O_{12}$	122738	C1C(C(OC2=C1C(=CC(=C2C3C(C(OC4=CC(=CC(=C34)O)O)C5=CC(=C(C=C5)O)O)O)O)O)C6=CC(=C(C=C6)O)O)O
38.	Rindoside	$C_{35}H_{42}O_{21}$	46174003	CC(=O)OCC1C(C(C(C(O1)OC2C(C3(CCOC(=O)C3=CO2)O)C=C)OC(=O)C)OC(=O)C)OC(=O)C4=C(C(=CC=C4)OC5C(C(C(C(O5)CO)O)O)O)O)O
39.	Orlistat	$C_{29}H_{53}NO_5$	3034010	CCCCCCCCCCCC(CC1C(C(=O)O1)CCCCCC)OC(=O)C(CC(C)C)NC=O

Table-2: Lipinski's RO5 study was using TargetNet showed 17 out of the 39 PCs (43.58%) satisfied all the rules

SL. NO	PHYTOCHEMICALS NAME	TPSA (Topological polar surface area) (<140)	MR (Molar Refractivity) (40-130)	MOLECULAR WEIGHT (<=500 D)	HBD-Hydrogen bond donor (<=5)	HBA1-Hydrogen bond acceptors (<=10)	LogP (<=5)	Lipinski rule of five
1.	Cyclopentasiloxane, Decamethyl	46.15	92.835	370.7697	0.0	10.0	3.592	75%
2.	Cyclohexasiloxane, dodecamethyl	55.38	111.402	444.92364	0.0	12.0	4.3104	75%
3.	Citronellol	20.23	50.8718	156.2652	1.0	1.0	2.7513	100%
4.	Isophytol	20.23	98.9798	296.531	1.0	1.0	6.3625	75%
5.	1,3-Cyclopentadiene, 5-(1-methylethylidene)-	0.0	37.034	106.165	0.0	0.0	2.4488	100%
6.	Phytol	20.23	98.9418	296.531	1.0	1.0	6.3641	75%
7.	Pyridine	12.89	24.237	79.0999	0.0	1.0	1.0816	100%
8.	Linolenic acid	37.3	88.9898	278.4296	1.0	2.0	5.6605	75%
9.	Oxyanthraquinone	80.39	66.1764	239.22616	2.0	4.0	2.331	100%
10.	dihydroxyanthraquinone	163.18	119.1754	444.48092	8.0	10.0	0.7886	50%
11.	epiafzelechin	90.15	72.3108	274.26866	4.0	5.0	1.8405	100%
12.	epicatechin	110.38	74.3338	290.26806	5.0	6.0	1.5461	75%
13.	Procyanidin B2	220.76	146.7126	578.52024	10.0	12.0	2.995	25%
14.	rhein	111.9	70.7543	284.22042	3.0	6.0	1.5714	100%
15.	rhein glucoside	191.05	102.8765	446.36102	6.0	11.0	-0.9555	50%
16.	sennoside A	347.96	202.796	862.73912	12.0	20.0	-1.0956	25%
17.	sennoside B	347.96	202.796	862.73912	12.0	20.0	-1.0956	25%
18.	chrysophanol	74.6	68.761	254.2375	2.0	4.0	2.1816	100%
19.	physcion	83.83	75.253	284.26348	2.0	5.0	2.1902	100%
20.	Kaempferol	111.13	76.012	286.2363	4.0	5.0	2.2824	100%
21.	Leucopelargonidin tetramer	279.68	278.731	1027.0294	12.0	16.0	11.1872	0.0%
22.	Fistulic acid	130.36	88.7043	358.29896	3.0	8.0	1.897	100.%
23.	Proanthocyanidins	229.99	147.5216	594.51964	10.0	13.0	2.7327	25%
24.	Catechin	110.38	74.3338	290.26806	5.0	6.0	1.5461	75%
25.	Diethyl Phthalate	52.6	58.615	222.23716	0.0	4.0	2.04	100%
26.	Cyanoacetylurea	95.98	27.3891	127.1014	2.0	5.0	0.18618	100%
27.	o-Veratramide	61.55	47.5209	181.18854	1.0	4.0	1.503	100%
28.	1,5-Diphenyl-2H-1, 2, 4-triazoline -3-thione	65.7	74.1847	253.32224	1.0	2.0	3.5969	100%
29.	Sarcosine	49.33	21.1085	89.09318	2.0	3.0	-0.3187	100%
30.	Patuletin	140.59	84.527	332.26168	5.0	7.0	1.9966	75%
31.	Methyl succinic acid	74.6	29.6926	132.11462	2.0	4.0	0.1818	100%
32.	Menisdaurin	143.4	71.964	313.30316	5.0	8.0	-2.05772	75%
33.	Robustaflavone	181.8	146.972	538.45792	6.0	8.0	5.134	25%
34.	1-Galloyl-Beta-D-glucose	177.14	71.4437	332.26014	7.0	10.0	-2.2399	50%
35.	Hydroxysafflor yellow A	34.14	67.52	224.25458	0.0	2.0	2.7243	100%
36.	Undulatoside A	149.82	83.6182	354.30872	5.0	8.0	-1.0143	75%
37.	Procyanidin B2	220.76	146.7126	578.52024	10.0	12.0	2.995	25%
38.	Rindoside	299.03	177.1415	798.69538	6.0	21.0	-2.0153	25%
39.	Orlistat	81.7	145.3637	495.73482	1.0	6.0	7.9087	75%

Table-3: Toxicity checking the phtocompounds using protox-ii tool

S.N.	Phytocompound	Tool	Toxic/Non-Toxic
1.	Citronellol	ProTox-II	NON-TOXIC
2.	1,3-Cyclopentadiene, 5-(1-methylethylidene)-	ProTox-II	NON-TOXIC
3.	Pyridine	ProTox-II	NON-TOXIC
4.	Oxyanthraquinone	ProTox-II	NON-TOXIC
5.	epiafzelechin	ProTox-II	NON-TOXIC
6.	rhein	ProTox-II	NON-TOXIC
7.	chrysophanol	ProTox-II	NON-TOXIC
8.	physcion	ProTox-II	NON-TOXIC
9.	Kaempferol	ProTox-II	NON-TOXIC
10.	Fistulic acid	ProTox-II	NON-TOXIC
11.	Diethyl Phthalate	ProTox-II	NON-TOXIC
12.	Cyanoacetylurea	ProTox-II	NON-TOXIC
13.	o-Veratramide	ProTox-II	NON-TOXIC
14.	1,5-Diphenyl-2H-1, 2, 4-triazoline -3-thione	ProTox-II	NON-TOXIC
15.	Sarcosine	ProTox-II	NON-TOXIC
16.	Methyl succinic acid	ProTox-II	NON-TOXIC
17.	Hydroxysafflor yellow A	ProTox-II	TOXIC

Prediction of Binding Site

The binding site of TRPV3 was identified by Computed Atlas of Surface Topography of Proteins (CASTp) [R-20]. The consensus results depict the active site residues that take part in the binding site formation.

Lipinski rule of five and Toxicity studies

Lipinski rule of five – Ro5

The RO5[R-21] states that (in *insilico* studies) any oral active drug should satisfy the rules such as Molecular mass (<=500 D), log P (<=5), Hydrogen bond donor (<=5), Hydrogen bond acceptors(<=10), Molar refractivity(40-130). This is the primary selection criteria. Violation of any one of the rule disqualifies the candidate compound as a potential source. Target Net web server [R-22] has been used to predict the RO5 for all the 39 PC's (http://targetnet.scbdd.com/calcnet/calc_rule_text/#**).**

Molecular Docking of PCs & reported drugs against TRPV3

Auto Dock, is a well-known molecular docking tool that is widely used for the screening of compounds against potential targets. We have used Auto Dock 4.2 tool [R-23] for molecular docking studies using computationally predicted and validated structure of TRPV3 against the 16non toxic PCs. The best-docked complexes were characterized and processed for further computational analysis based on binding energy values, ligand efficiency, intermolecular hydrogen (H)-bonds, and other hydrophobic and electrostatic interactions. For topical levity 5 commercial allopathic drugs namely, Coaltar [R-25], Acitrtin [R-26], Calcipotriol [R-27], Tazarotene [R-28] and 'Nelarabine'(liquid cancer drug repurposed as anti-psoriasis) [R-29] have been presented.

RESULTS

The gene TRPV3 is the most common and predominant in psoriasis. It is also involved in hypersensation and in psoriatic pruritus. Hence, TRPV3 has been taken for the study. The crystal structure of TRPV3's protein was collected from RCSB PDB pdb id 6dvz [R-29]. The chain A of the structure was selected for in silico investigation. From castp web server the binding site of the protein were obtained.The binding sites predicted of the protein are as follows : LYS 253, TYR524, THR937,ASP400,ASN401,GLU405, ILE406, VAL408, TYR 409,ASN410,THR 411,ASN412, ARG416, PHE 441, SER444, PHE447, TYR448, TYR451, TRP493,CYS496, ILE497, LYS500, GLU501, ILE503, ALA504, LEU507,LEU508, ARG509, PRO510,ASP512, LEU513, GLN514, SER515, ILE516, ASP519, ALA520, PHE 522, HIS523, PHE524, PHE526, PHE527,ALA564, TYR565, ARG567, LEU594, GLN695, ARG698, THR699, LEU701, GLU702, GLU704, LYS705 and MET706. The grid box value taken for the study is with X-dimension = 76, Y-dimension = 110 and Z-dimension =98 with spacing 0.375 Angstrom.

Molecular docking

The binding free energies of TRPV3 with all the 16 screened PCs and 5 commercially available allopathic drugs namely**,** Coaltar, Acitrtin, Calcipotriol, Tazarotene and Nelarabine interaction complexes are presented in Table 4 and Table 5, respectively. Out of the 16 PCs from *Cassia fistula* 3 PCs showed higher binding affinity. Chrysophanol showedthe highest@ -7.58 kcal/mol, followed by Oxyanthraquinone with-6.77 kcal/mol and Rhein -6.73 kcal/mol., respectively. Figure 2 shows the 2D and 3D structures of Chrysophanol. Figure 3 and 4 shows the 2D and 3D structure of Chrysophanolrespectively. Figure 5 and 6 shows the 2D and 3D interaction of TRPV3 protein and Oxyanthraquinone respectively. Figure 7 and 8 shows the 2D and 3D interaction of TRPV3 protein and Rhein Complex respectively. Among the 4 anti-psoriasis allopathic drugs, Tazarotene showsan high binding affinity of -7.82 kcal/mol. However, ithas only 1'H' atom = bonding uncertainty. Similarly, Nelarabine the re-purposed drug has an binding affinity of only -4.11 kcal/molwhich is less by an order ranging between 80-95 % vis-à-vis Chrysophanol, Oxyanthraquinone& Rhein..And Calcipotriol is found to be toxic via ProTox-II server test (Table - 6).

Table-4: Docking of screened Compounds from Cassia fistula against TRPV3 protein of Psoriasis

Sl. No.	Phytocompound	Binding Energy(kcal/ Mol)	Ligand Efficiency	Inhibition Constant (µm)	No. of H Bonds	H-Bond Forming Residues	Average Distance of H-Bonds (Å)
1.	Citronellol	-3.63	-0.33	2.17	2	LYS705,GLU405	2.506685
2.	1,3-Cyclopentadiene, 5-(1-methylethylidene)-	-4.18	-0.52	858.34	N/A	N/A	N/A
3.	Pyridine	-3.43	-0.57	3.06	N/A	N/A	N/A
4.	Oxyanthraquinone	-6.77	-0.38	10.84	3	HIS426,LEU420, ARG693	2.485776667
5.	epiafzelechin	-6.04	-0.3	37.19	4	TYR409,LYS500	2.7273075
6.	Rhein	-6.73	-0.32	11.7	2	HIS426,ARG693	2.34932

7.	Chrysophanol	-7.58	-0.4	2.8	3	HIS426,LEU420	2.378486667
8.	physcion	-6.25	-0.3	26.21	1	HIS417	2.54824
9.	Kaempferol	-6.4	-0.3	20.41	4	LYS705,GLU405, PRO510,ASN410	2.1602375
10.	Fistulic acid	-6.71	-0.26	11.98	4	TRP433,PHE569, ARG696	3.0264625
11.	Diethyl Phthalate	-5.0	-0.31	215.98	1	HIS430	2.8415
12.	Cyanoacetylurea	-4.85	-0.54	280.84	3	GLU704,THR397	2.076243333
13.	o-Veratramide	-3.88	-0.3	1.44	1	ALA560	2.00649
14.	1,5-Diphenyl-2H-1, 2, 4-triazoline -3-thione	-5.79	-0.32	56.96	N/A	N/A	N/A
15.	Sarcosine	-3.55	-0.59	2.52	3	LYS705,GLU405	2.263403333
16.	Methyl succinic acid	-5.79	-0.64	56.56	1	LYS435	2.77716

Table-5: Docking of Allopathic Licenced Drug Moieties against TRPV3 protein of Psoriasis

Sl. No.	Phytocompound	Binding Energy (kcal/Mol)	Ligand Efficiency	Inhibition Constant (µm)	No. of H Bonds	H-Bond Forming Residues	Average Distance of H-Bonds (Å)
	Nelarabine (FDA APPROVED DRUG REPORTED)	-4.11	-0.2	972.2	3	ARG567,GLU501, PHE522	2.552373333
	coal tar	-6.57	-0.47	15.38	N/A	N/A	N/A
	acitretin	-7.51	-0.31	3.13	1	ASP519	2.0084
	Calcipotriol	-7.68	-0.26	2.33	2	TYR565,ALA564	2.151095
	Tazarotene	-7.82	-0.31	1.86	1	ARG567	3.28192

Table-6: TOXICITY off Table 5 members via ProTox-II tool

S.N.	Phytocompound	Tool	Toxic/Non-Toxic
1.	Nelarabine (FDA APPROVED DRUG REPORTED)	ProTox-II	NON-TOXIC
2.	coal tar	ProTox-II	NON-TOXIC
3.	acitretin	ProTox-II	NON-TOXIC
4.	Calcipotriol	ProTox-II	TOXIC
5.	Tazarotene	ProTox-II	NON-TOXIC

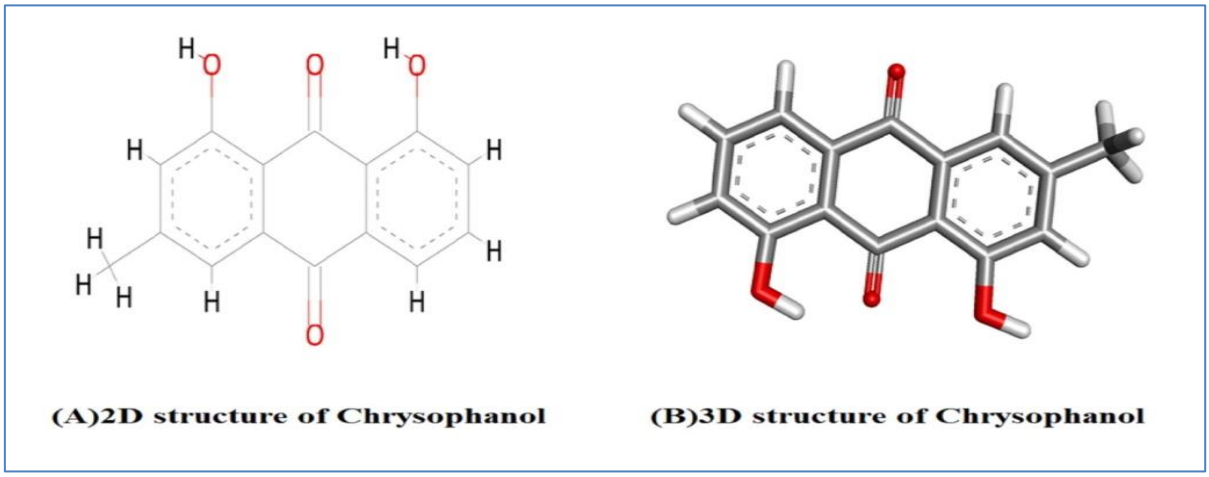

Fig-2: Shows the 2D and 3D structure of Chrysophanol

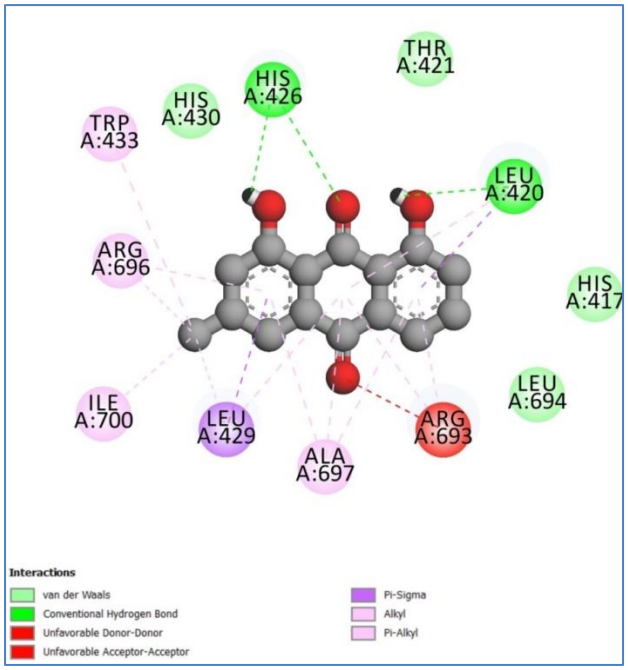

Fig-3: Shows the 2D interaction of TRPV3 protein and Chrysophanol Complex

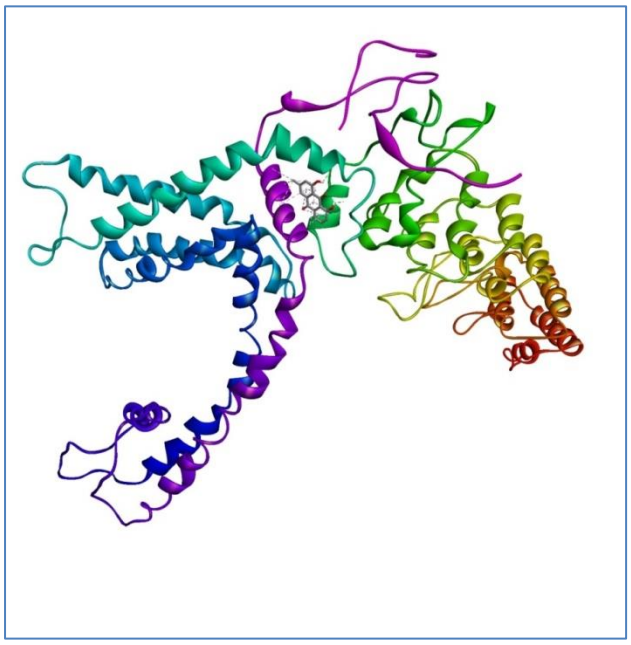

Fig-4: Shows the 3D interaction of TRPV3 protein and Chrysophanol Complex

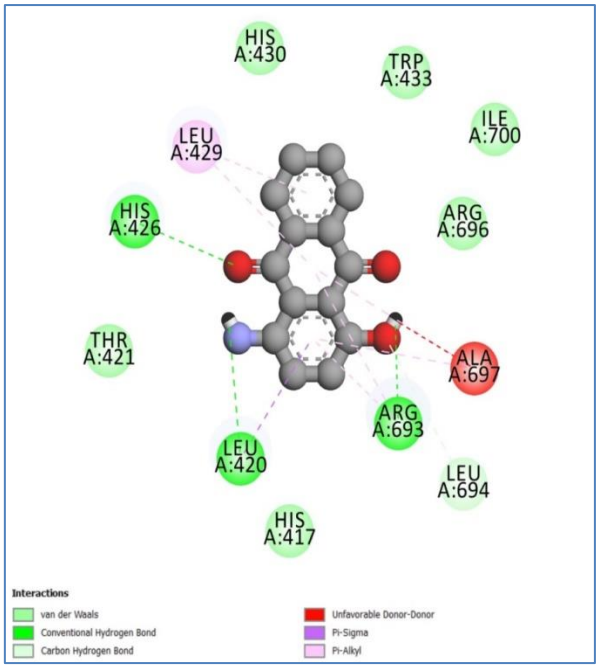

Fig-5: Shows the 2D interaction of TRPV3 protein and Oxyanthraquinone Complex

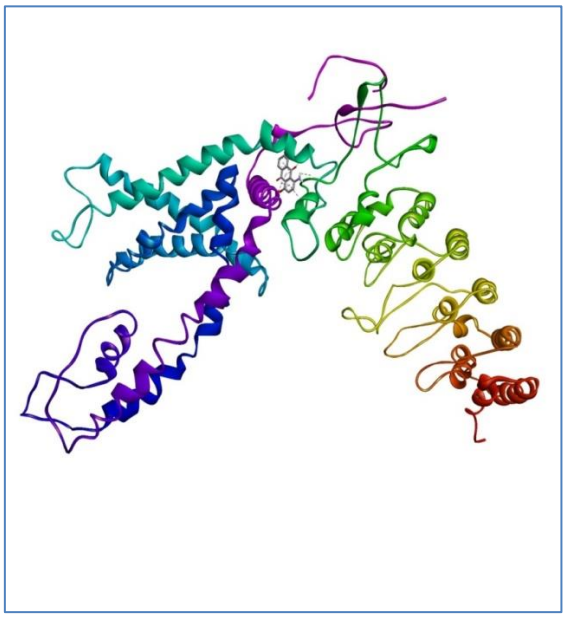

Fig-6: Shows the 3D interaction of TRPV3 protein and Oxyanthraquinone Complex

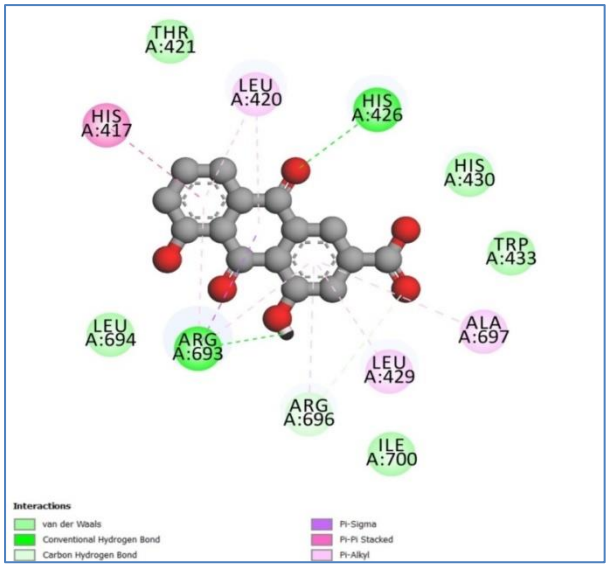

Fig-7: Shows the 2D interaction of TRPV3 protein and Rhein Complex

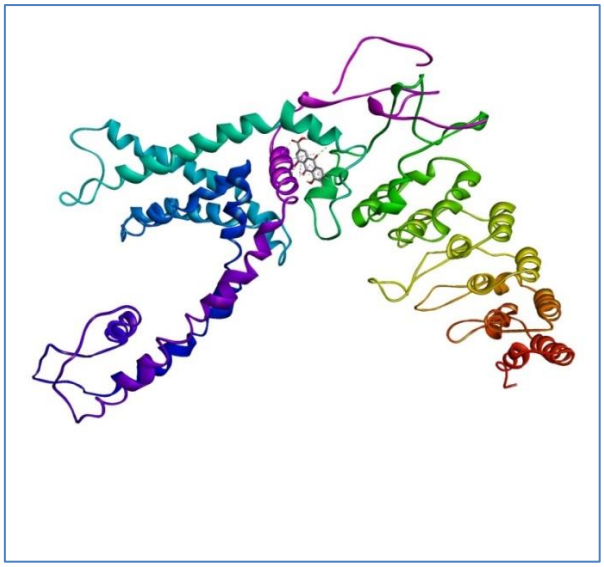

Fig-8: Shows the 3D interaction of TRPV3 protein and Rhein Complex

Table-7: Suggestive Multi-Disciplinary Versatile Therapeutic Method (Model).

For*	Nelarabine [a]	Chrysophanol [b]	Rhein [c]	Tazarotene [d]	Admix [e]	C. fistula [f]	Form #
1 [a]	**300 mg/ m²**	**xx**	**xx**	**xxx**	'a' is administered IV as in 'a' + an admixture of b+c+d orally as in 'b'	xx	**IV**
2[b]	As IV with Nor Sal @ 500ml. + others Currently used standalone re-purposed therapy.	**100-300 mcg** 'a & b' only. Orally. Admixed with Banana or sweet corn porridge or sugar cane jiggery as buffering food. Range: clinical assessment basis.	**xxx**	**xx**		**500mg** Dry powder; bark\any other along with 'a'	**FD-T\C**
3[c]			**100-300 mcg**	**xx**			-Do-
4[c]			'a & c' only. Rest : as in 'b'	**100-300 mcg**			-Do-
5[d]				'a & d' only. Rest : as in 'c'			-Do-
6[e]					**xx**		-Do-

For* = Formulation. Mg =milligram; mcg = micro gram; IV = intravenous. FD-T\C = fixed dose tablet\Capsule. More works on.

Table – 7 gives a suggestive therapeutic method. It is complementing compound based holistic and functional food concept. Nelarabine 'a' = a chemotherapy medication used for the treatment of T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma i.e., autosomal recessive diseases marked by Purine nucleoside phosphorylase deficiency which is addressed by IV infusion of Nelarabine. Repurposed usage; expensive; case specific complication\delayed side effects. Nevertheless, Soriasis returns (there is however no reports\instances of Rebound phenomena). Chrysophanol 'b' = used for cooling blood (circulation control to an inflamed brain, & bowl loop relaxing. Rhein 'c'= (protector of systemic physiological processes) viz., is hepato-protective, nephro-protective, anti-cancer, anti-inflammatory, and several other protective effects; versatile. Tazarotene 'd'= already being used to treat Psoriasis; dermis target molecule (vital for our objectives). Nelarabine (no indulgence) is only a representative candidate any of the known anti-soriasis medication can benefit due to concurrent use of C.Fistula as functional food (home made-hand made) and extra mural nursing [29;30]. Using Nano-Technology such unique combination can be formulated as a mini pill Fixed Dose [31].

NOTE: *Nelarabine is only a case study candidate to highlight the scenario of "mixo-pathy" i.e., complementing application of synergistic items with family welfare as the objective. No commerce. No indulgence. That, e.g., Formulation 'f' a toxic moiety can be repurposed for use@ 1/3rd potency further tapered to a single infusion for 3 continuous months (30 days interval in-between each sub-clinical IV dosing) in hospital setting while C Fistula bark powder (made sterile by Gamma radiation @ 20 Kilo Gray) can be orally chewed taken/as a capsule @ 500mg daily for all the 90 days therapy period.*

Atomic Composition Comparison

Fig-9 is the Graph of the atomic composition Chrysophanol: C15H10O4, Molar mass: 254.24 (Blue); Rhein: C15H10O5; 284.22042 (Maroon) and Oxyanthraquinone: C27H32O3 239.22616 (Green). Chrysophanol and Rhein (maroon) suggest inter-

synergy. Oxyanthraquinone(green) posits as member inhibitor.

Fig-10 is the Graph of the atomic composition of Coaltar: assumed as 000 (Blue) {*}, Acitrtin: C21H26O3, (Meroon); Calcipotriol: C27H40O3, Tazarotene: C21H21NO2S (Green); and Nelarabine C11H15N5O5 (Violet). Tazarotene (green) posits as the broad spectrum efficacy inducer cum potency up-regulating member. Chrysophanol and Rhein double up as process scavengers (*). CT has more than 1000 compounds ! hence we have assumed hypothetical values of C0H0O0 for its structure.

Juxtaposing the results of Fig-9 & Fig 10 prima facie an clinical synergy is suggested between Nelarabine and PCs *Chrysophanol* and Rhein as functional food\adjuncts and Tazarotene potency up-regulating cum in-blood life lengthening member (others, variedly).

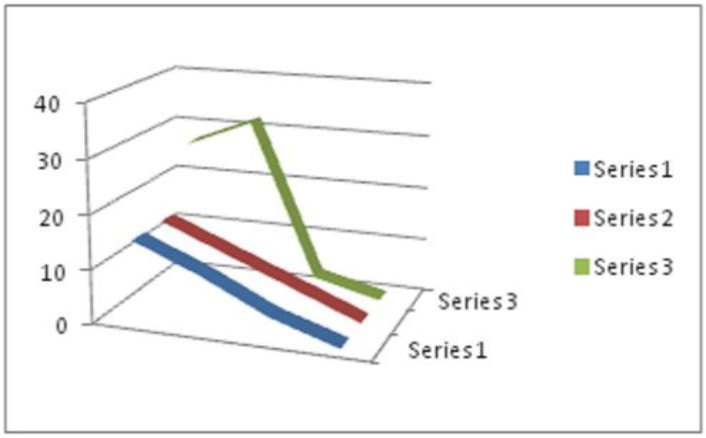

Fig-9: The Graph of the atomic composition Chrysophanol: C15H10O4, (Blue); Rhein : C15H10O5; 284.22042 (Maroon) and Oxyanthraquinone : C27H32O3&239.22616(Green). Chrysophanol and Rhein (maroon) suggest inter-synergy. Oxyanthraquinone (green) posits as member inhibitor

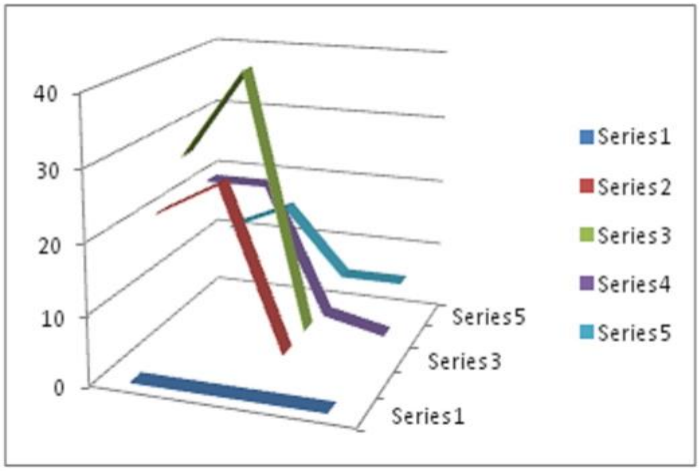

Fig-10: The Graph of the atomic composition of Coal tar: assumed as 000 (Blue) {*}, Acitrtin: C21H26O3, (Meroon); Calcipotriol: C27H40O3, Tazarotene: C21H21NO2S (Green); and Nelarabine C11H15N5O5 (Violet). Tazarotene (green) posits as the broad spectrum efficacy inducer cum potency up-regulating member. Chrysophanol and Rhein doubling up as process scavengers (*). CT has more than 1000 compounds ! hence we have assumed hypothetical values of C0H0O0 for its structure

DISCUSSION & THEORY

Atoms are important in affecting bonding and the most vital being 'H' atom. Although Oxyanthraquinone have higher 'H' atoms, it is the presence of heavy atoms that down regulates its bonding affinity. The electro-negativity of the C atoms is as much as that of the H atoms. C withdraws the majority of the electrons from the electron dense covalent bond with the H's leaving the H atom electron-deficient [33]. Thus the electron depleted H atom thence is as alike an bare proton (large mass vagabond member), susceptible to wandering & bond unpredictability [34;35] this is of special relevance in poly-morphysim in neoplasias. C is also a heavy member as compared to H. Additionally becauses degeneration of the H ion potential. If the C atoms in Oxyanthraquinone could be reduced to <16 then it will indicate nice affinity. The presence of S in Tazarotene enhances binding potential while N atom in Nelarabine thwarts bonding affinity and also exponentially raises

the disassociation constant.Removalof N atoms shall downturn the electro-negativity of this drug (making it more effective clinically in liquid cancers & psoriasis) and up-regulate Nelarabine's efficacy to greater than Chrysophanol; and still more with addition of S. Nitrogen is the principal cause of Nelarabine's large disassociation constant. Greater the disassociation less is the therapeutic consistency (inverse relationship). S has also been known for long as of having efficacy in dermal pathologies. This in-silico study vets it further.

In anthropogenic physiological processes the lower be the binding energy the quicker be the docking and if the inhibition constant also be low then the intermolecular binding 'likeness' enlarges. Finally if the 'H' bond's distance be less or of equal order (vis-à-vis known clinical compounds) it further matters much in process efficacy. This is because an H atom which is the driver ion cum bond signaling potential member has a variable diameter of < 75ppm (100ppm = 1 angstrom). Thus, Chrysophanol & Calcipotriol severally have more electron load in the inter-molecular bonds (space) resulting in better and failsafe docking and jointly shall indicate high clinical efficacy and strong anti-inhibition (viz., chronic status systemic pathogenic and systemic response mediated inhibitions). From such parameters, Chrysophanol; and Rhein (Table-4) score well among the PCs so also all the allopathic members as are in Table-5.

CONCLUSION

Chrysophanoland Rhein(Sl. No. 6,7 of T- 4) posit as the champion and runners-up respectively in this computational study. Chrysophanolshows the highest binding affinity against TRPV3. It is toxicologically safe. Indicates good efficacy at low potencies. Repurposed drug Nelarbine stands a good chance for re-engineering for better efficacy with greater safety indications (applicable also in its present naïve form). The trio can be expected as future anti-psoriasis drug candidates; starting material; SOS application; etc. Existing anti-psoriasis conventional drugs are likely to yield results whence Chrysophanoland\or Rheinare co-administered as functional food or as therapeutic/s on fixed dose basis. Even MDT (multi-drug therapy) approach posits promising being comprised of any of the members of Table-5 + Nelabrine + Chrysophanoland\or Rhein as functional food or as adjunct herbal medicament. S stands validated in dermal pathologies. N not. Oxyanthraquinone is discounted as there is a barrier\inhibition between it & Chrysophanol (correlate with Fig-3). Table – 7 is helpful for the (i) Family Physician (ii) small manufacturers (iii) local sustainable employment creation (iv) reduce Carbon Foot Print. This study is noncommercial; is indicative; not exhaustive.

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DECLARATIONS OF INTEREST

Authors declare that they have no conflict of interest. This study is noncommercial; not funded; non donor driven.

REFERENCES

1. Richardson, S. K., & Gelfand, J. M. (2008). Update on the natural history and systemic treatment of psoriasis. *Advances in dermatology*, 24, and 171.
2. American academy of Dermatology. (https://www.aad.org/public/diseases/psoriasis/what/causes#:~:text=When%20a%20person%20has%20psoriasis, skin%2C%20and%20you%20see%20psoriasis.)
3. Pawar, A. V., & Killedar, S. G. (2017). Uses of Cassia fistula Linn as a medicinal plant. *International Journal for Advance Research and Development*, *2*(3).
4. Szallasi, A. (Ed.). (2015). TRP channels as therapeutic targets: from basic science to clinical use. Academic Press.
5. Jothy, S. L., Zakaria, Z., Chen, Y., Lau, Y. L., Latha, L. Y., &Sasidharan, S. (2011). Acute oral toxicity of methanolic seed extract of Cassia fistula in mice. *Molecules*, *16*(6), 5268-5282.
6. Charak Samhita c.4th A.D., of Agnivesa, Bramhanand Tripathy ed., 2 Vols. (1969). Chaukhamba Surabharati Prakashan, Varanasi, 1973. AND Charak Saamhita of Agnivesh, 2Vols., Ed. Kashinath Sastri and Gorakhnath Chaturvedi, Chowkhamba Vidyabhavan,Varanasi.
7. Bhattacharya, D. (2014). Select Palm Leaf Manuscripts Of Health Care Sciences, *Indian Journal of History of Science, Indian National Science Academy*, *49*(3), 294-97.
8. Read, B. E., & LI, S. C. (1936). Chinese Medicinal Plants from the Pen Ts' ao Kang Mu [of Li Shih-chên]... of a Botanical, Chemical and Pharmacological Reference List, Etc. Peking natural history bulletin.
9. Ayurvedic, P. (2016). AYUSH, govt of india, pharmacopoeia commission for indian medicine …, Extracts (monograph), Part-I, 9, 95-98. https://www.easyayurveda.com/2016/05/11/indian-senna-cassia-angustifolia/.
10. TheAyurvedic Formulary of India Part-I vol-VI, 2nd Edition. (2003). The Controller of publications, Govt. of India, Civillines, New Delhi.
11. Rastogi, R. P., & Mehrotra, B. N. (1999). Compendium of Indian Medicinal Plants Central

Drug Research institute Luck now and National institute of Science communication. New Delhi, 280.
12. Hari, Om. S., & Brahmam, M. (1994). *The Flora of Orissa*, 4 vols. RRL, CSIR, Bhubaneswar, (2198 pages).
13. Sharma, P. C., Yelne, M. B., Dennis, T. J., Joshi, A., &Billore, K. V. (2000). Database on medicinal plants used in Ayurveda.
14. Kim, S., Thiessen, P. A., Bolton, E. E., Chen, J., Fu, G., Gindulyte, A., & Bryant, S. H. (2016). PubChem substance and compound databases. *Nucleic acids research*, *44*(D1), D1202-D1213.
15. Kulkarni, A., Govindappa, M., Ramachandra, Y. L., & Koka, P. (2015). GC-MS analysis of methanol extract of Cassia fistula and its in vitro anticancer activity on human prostate cancer cell line. *Indo Am J Pharm Res*, *5*(2), 937-44.
16. Bahorun, T., Neergheen, V. S., &Aruoma, O. I. (2005). Phytochemical constituents of Cassia fistula. *African journal of Biotechnology*, *4*(13).
17. Bhagyashree, B., Namdev, G., Supriya, M., Ramesh, K., Suhas, P., & Sankunny. M. K. (2018). Efficacy of Methanol Extract of Cassia Fistula Linn Stem Bark against Different Virulence Factors of the Human Pathogen Candida albicans.
18. Aabideen, Z. U., Mumtaz, M. W., Akhtar, M. T., Raza, M. A., Mukhtar, H., Irfan, A., & Saari, N. (2021). Cassia fistula Leaves; UHPLC-QTOF-MS/MS based metabolite profiling and molecular docking insights to explore bioactives role towards inhibition of pancreatic lipase. *Plants*, *10*(7), 1334.
19. Kiss, R., Sandor, M., &Szalai, F. A. (2012). http://Mcule. Com: a public web service for drug discovery. *Journal of cheminformatics*, *4*(1), 1-1.
20. Binkowski, T. A., Naghibzadeh, S., & Liang, J. (2003). CASTp: computed atlas of surface topography of proteins. *Nucleic acids research*, *31*(13), 3352-3355.
21. Lipinski, C. A. (2004). Lead-and drug-like compounds: the rule-of-five revolution. *Drug discovery today: Technologies*, *1*(4), 337-341.
22. Yao, Z. J., Dong, J., Che, Y. J., Zhu, M. F., Wen, M., Wang, N. N., & Cao, D. S. (2016). Target Net: a web service for predicting potential drug–target interaction profiling via multi-target SAR models. *Journal of computer-aided molecular design*, *30*(5), 413-424.
23. Lokesh, R., & Kannabiran, K. (2016). A handbook on protein ligand docking tool: autodock4.
24. Ibezim, A., Onah, E., Dim, E. N., & Ntie-Kang, F. (2021). A computational multi-targeting approach for drug repositioning for psoriasis treatment. *BMC Complementary Medicine and Therapies*, *21*(1), 1-8.
25. Bhatia, A., Singh, B., Amarji, B., Negi, P., Shukla, A., &Katare, O. P. (2011). Novel stain-free lecithinized coal tar formulation for psoriasis. *International journal of dermatology*, *50*(10), 1246-1248.
26. Carretero, G., Ribera, M., Belinchón, I., Carrascosa, J. M., Puig, L., Ferrandiz, C., & Psoriasis Group of the AEDV. (2013). Guidelines for the use of acitretin in psoriasis. *Actas Dermo-Sifiliográficas (English Edition)*, *104*(7), 598-616.
27. Scott, L. J., Dunn, C. J., & Goa, K. L. (2001). Calcipotriol ointment. *American journal of clinical dermatology*, *2*(2), 95-120.
28. Duvic, M. (1997). Tazarotene: a review of its pharmacological profile and potential for clinical use in psoriasis. *Expert opinion on investigational drugs*, *6*(10), 1537-1551.
29. Ibezim, A., Onah, E., Dim, E. N., &Ntie-Kang, F. (2021). A computational multi-targeting approach for drug repositioning for psoriasis treatment. BMC Complementary Medicine and Therapies, 21(1), 1-8.
30. Agrawal, A., & Kulkarni, G. T. (2020). Molecular docking study to elucidate the anti-pruritic mechanism of selected natural ligands by desensitizing TRPV3 ion channel in Psoriasis: An in silico approach. *Indian Journal of Biochemistry and Biophysics (IJBB)*, *57*(5), 578-583.
31. Bhattacharya, D. (2017). Nursing Defeats Cancer, *Jor of Nursing & Health Care*, *5*(3), (juniper); https://juniperpublishers.com/jojnhc/archive.php
32. Bhattacharya, D. (2021). Covid Nursing: Less Known Aspects. *Saudi J Nurs Health Care. 4(*10); 317-332. https://saudijournals.com/media/articles/SJNHC_410_317-332_810dT0H.pdf
33. Bhattacharya, D. (2017). Nano Tech Tablet: A Concept, *Novel Approaches In Drug Designing & Approaches*, *2*(2).
34. Mavroyannis, C., & C. A. Winicler. (1962). The Reaction of Nitrogen Atoms with Hydrogen Atoms, Upper Atmosphere Chemistry Research Group, *the Canadian Journal of Chemistry*, 40, 240-45. McGill University, Montreal, Quebec. https://cdnsciencepub.com/doi/pdf/10.1139/v62-041.
35. https://courses.lumenlearning.com/cheminter/chapter/hydrogen-bonding/#:~:text=Hydrogen%20bonding%20occurs%20only%20in,H%20atom%20very%20electron%2Ddeficient