Supplementary Information

Synthesis and evaluation of isatin-N-1,2,3-triazoles analogues for *in vitro* anticancer, α-glucosidase inhibition properties *via* molecular hybridization approach

A Niranjana Kumar[a], J Kotesh Kumar*[a], K V N S Srinivas*[a], Srinivas Chinde[b], Anand Kumar Domatti[c], Yogesh Kumar[d], Paramjit Grover[b], Ashok Tiwari[c] & Feroz Khan[d]

[a] Phytochemistry Division, CSIR-Central Institute of Medicinal and Aromatic Plants, Research Centre, Boduppal, Hyderabad 500 092, India

[b] Toxicology Unit, Biology Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India

[c] Medicinal Chemistry and Pharmacology Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India

[d] Metabolic and Structural Biology Department, CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow 226 015, India

E-mail: koteshkumarj.cimap@csir.res.in, kvnsatyasrinivas.cimap@csir.res.in

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Other docking studies Supplementary data

Table S8: Compliance of Acarbose, Doxorubicin, Orlista, isatine and its derivatives to the computational parameters of oral bioavailability (Lipinski's rule of five).

S.No.	Molecular Weight (<500)	ALogP (≤5)	Number H Donors (≤5)	Number H Acceptors (≤10)	Molecular Fractional Polar Surface Area (≤140Å^2)	Number of violations
Acarbose	645.626	-6.839	14	19	0.537	3
Doxorubicin	543.536	-0.044	6	12	0.408	3
Orilistat	495.75	8.333	1	5	0.152	1
1	147.135	0.67	1	2	0.348	0
3a	365.353	0.528	2	7	0.336	0
3b	346.349	2.174	0	5	0.266	0
3c	365.353	0.049	2	7	0.338	0
3d	352.783	3.105	0	4	0.215	0
3e	387.228	3.769	0	4	0.2	0
3f	336.328	2.646	0	4	0.225	0
3g	336.328	2.646	0	4	0.225	0
3h	343.348	2.319	0	5	0.284	0
3i	419.446	3.838	0	5	0.234	0

Footnote: LogP = octanol/water partition coefficient, a measure for lipophilicity.

Table S9: Compliance of Acarbose, Doxorubicin, Orlista, isatine and its derivatives to the computational parameters of pharmacokinetics (ADME

S.No.	ADMET EXTCYP2D6 Prediction	ADMET EXT Hepatotoxicity Prediction	ADMET Absorption_ Level	ADMET EXT PPB Prediction	ADMET BBB Level
Acarbose	FALSE (non-inhibitor)	FALSE (non-toxic)	3 (good)	FALSE (poorly bounded)	4 (undefined)
Doxorubicin	FALSE (non-inhibitor)	TRUE (toxic)	3 (good)	FALSE (poorly bounded)	4 (undefined)
Orilistat	FALSE (non-inhibitor)	FALSE (non-toxic)	3 (good)	TRUE (highly bounded)	4 (undefined)
1	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	FALSE (poorly bounded)	3 (poor)
3a	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	4 (undefined)
3b	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	3 (poor)
3c	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	4 (undefined)
3d	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	2 (medium)
3e	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	2 (medium)
3f	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	2 (medium)
3g	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	2 (medium)
3h	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	3 (poor)
3i	FALSE (non-inhibitor)	TRUE (toxic)	0 (poor)	TRUE (highly bounded)	2 (medium)

Abbreviations: CYP450 cytochrome P450, PPB plasma protein binding, BBB blood brain barrier

Table S10 (a): Compliance of Acarbose, Doxorubicin, Orlista, isatine and its derivatives to computational parameters of USFDA (a) rodent carcinogenicity (mouse male/female and Rat male/female), WOE Prediction, Ames mutagenicity (b) developmental toxicity potential (DTP), skin Irritancy, skin sensitization, ocular irritancy, skin irritancy and aerobic biodegradability.

S.No.	TOPKAT Mouse Female FDA	TOPKAT Mouse Male FDA	TOPKAT Rat Female FDA	TOPKAT Rat Male FDA	TOPKAT WOE Prediction	TOPKAT Ames Prediction
Acarbose	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Mutagen
Doxorubicin	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Mutagen
Orilistat	Non-Carcinogen	Multi-Carcinogen	Single-Carcinogen	Multi-Carcinogen	Non-Carcinogen	Non-Mutagen
1	Non-Carcinogen	Single-Carcinogen	Multi-Carcinogen	Multi-Carcinogen	Carcinogen	Mutagen
3a	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Non-Mutagen
3b	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Mutagen
3c	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Non-Mutagen
3d	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Mutagen
3e	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Mutagen
3f	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Non-Mutagen
3g	Non-Carcinogen	Non-Carcinogen	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Non-Mutagen
3h	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Multi-Carcinogen	Carcinogen	Non-Mutagen
3i	Non-Carcinogen	Single-Carcinogen	Non-Carcinogen	Multi-Carcinogen	Carcinogen	Non-Mutagen

Abbreviations: USFDA, United States Food and Drug Administration

Table S10 (b):

S.No.	TOPKAT DTP Prediction	TOPKAT Skin Irritancy	TOPKAT Skin Sensitization	TOPKAT Ocular Irritancy	TOPKAT Aerobic Biodegradability Prediction
Acarbose	Toxic	Mild	Weak	Severe	Degradable
Doxorubicin	Toxic	None	Weak	Mild	Non-Degradable
Orilistat	Non-Toxic	Moderate	None	None	Degradable
1	Non-Toxic	None	Strong	Moderate	Non-Degradable
3a	Non-Toxic	None	Strong	Mild	Non-Degradable
3b	Non-Toxic	None	Strong	Mild	Degradable
3c	Non-Toxic	None	Strong	Mild	Non-Degradable
3d	Non-Toxic	None	Strong	Mild	Non-Degradable
3e	Non-Toxic	None	Strong	Mild	Non-Degradable
3f	Non-Toxic	None	Strong	Mild	Non-Degradable
3g	Non-Toxic	None	Strong	Mild	Non-Degradable
3h	Non-Toxic	None	Strong	Mild	Non-Degradable
3i	Non-Toxic	None	Strong	Mild	Non-Degradable

Table S11: Compliance of Acarbose, Doxorubicin, Orlista, isatine and its derivatives to computational parameters of USFDA Carcinogenic Potency TD_{50} Mouse, Carcinogenic Potency TD_{50} Rat, Rat Oral LD_{50}, Chronic LOAEL and Fathead Minnow LC_{50}.

S.No.	TOPKAT Carcinogenic Potency TD_{50} Mouse, mg/kgbodyweight/day	TOPKAT Carcinogenic Potency TD_{50} Rat, mg/kgbodyweight/day	TOPKAT Rat Oral LD_{50}, g/kgbodyweight	TOPKAT Rat Inhalational LC_{50}, mg/m3/h	TOPKAT Chronic LOAEL, g/kgbodyweight	TOPKAT Fathead Minnow LC_{50}, g/l
Acarbose	0.647263	0.14123	11.1218	0.00121286	0.0242445	5,621.70
Doxorubicin	6.97341	0.655332	0.310213	0.0752162	0.0132164	0.26038
Orilistat	232.025	2.27455	12.0711	6.38876	0.0456907	1.05E-07
1	494.979	177.405	1.81104	2.58357	0.345805	0.142513
3a	27.0682	23.2428	17.7183	3.71358	0.152442	0.100971
3b	82.6993	37.2456	3.50205	6.09741	0.141202	0.00310519
3c	16.2059	27.4147	31.2582	1.61917	0.205016	0.0978481
3d	34.8942	21.2265	1.87539	7.02146	0.0983871	0.00108338
3e	48.8067	20.8707	1.73925	5.94773	0.0803824	0.000370058
3f	31.2932	21.891	1.03153	7.73979	0.0984903	0.00212087
3g	53.5648	21.891	1.51249	7.20741	0.0885133	0.00212087
3h	61.0369	25.174	1.86631	1.89234	0.108843	0.00204038
3i	10.7633	3.61516	2.39018	1.87263	0.0796433	0.000149039

References

Niranjana Kumar A, Smruti Ranjan D, Kotesh Kumar J, Srinivas KVNS, Sarada DT. 2025. Design and development of an isatin-1,2,3-triazole hybrid analogue as a potent anti-inflammatory agent with enhanced efficacy and gene expression modulation. RSC Adv., 15, 2023–2033. DOI: 10.1039/d4ra07294d.