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GC-MS Profiling of Phytocompounds in White Pumpkin Seed Extract, Pharmacokinetic and Toxicity Properties by ADME/Tox Analysis

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White pumpkin (*Benincasa hispida*) seeds contain diverse phytocompounds with medicinal relevance. This study profiled metabolites in the methanolic seed extract by gas chromatography–mass spectrometry (GC-MS) and assessed pharmacokinetic and toxicity properties using *in silico* ADME/Tox tools. Twenty-one phytocompounds were identified, conquered by fatty-acid esters and phytosterols; the most abundant were 9,12-octadecadienoic acid, methyl ester (20.9%) and γ-sitosterol (14.0%). Predicted drug-likeness and oral developability were generally favourable for the fatty-acid esters (high gastrointestinal absorption, limited safety liabilities), whereas sterols showed lower gastrointestinal absorption but acceptable toxicity signals.

Keywords: *Benincasa hispida*, White pumpkin seed, Phytosterols, ADME, Toxicity prediction.

INTRODUCTION

Benincasa hispida (white pumpkin/ash gourd) seeds are widely consumed in Asia and valued for nutrition and traditional medicine. Recently, GC-MS analysis on *B. hispida* and related cucurbits shows that seed extracts are rich in unsaturated fatty acids (notably linoleic acid), fatty-acid esters and other bioactive compounds that can underpin anti-inflammatory and antioxidant effects [1]. In particular, GC-MS profiles of *B. hispida* and *Cucurbita moschata* seeds consistently report 9,12-octadecadienoic acid (Z,Z) and its methyl esters as dominant constituents, alongside *n*-hexadecanoic acid and related lipids that are relevant to food and health applications [1].

Pumpkin seed oil (PSO) is a well-studied functional lipid source; replacing saturated fats with polyunsaturated fatty acid (PUFA)-rich PSO improves dyslipidaemia and attenuates non-alcoholic fatty liver disease (NAFLD) and atherosclerosis in preclinical models, with virgin (unrefined) PSO conferring additional anti-inflammatory benefits due to its phytochemical fraction [2]. Beyond cardiometabolic endpoints, clinical and translational studies suggest broader utility, for example, trans-perineal PSO phonophoresis improved symptoms and urinary parameters in chronic non-bacterial prostatitis [3], while plant derived squalene (a triterpene present in seed oils) formulated as a microemulsion showed acceptable safety and signals of benefit in a randomized COVID-19 cohort, together illustrating the therapeutic promise of lipidic seed constituents [4]. From a techno-functional standpoint, pumpkin seed proteins exhibit useful structuring behaviour in foods, *e.g.* co-gelation of pumpkin-seed protein with egg-white protein enhances gel elasticity, hardness, and water binding, which attributes valuable for texture design and special-needs nutrition [5]. Such protein–protein systems align with recent work showing that egg-white/pumpkin-seed protein composites can be tuned for swallowing functionality in dysphagia-friendly foods [5]. Moreover, valorization of pumpkin byproducts (seed/pomace) supports circular bioeconomy aims; in aquaculture, pumpkin pomace improved feed conversion and antioxidant status of *Penaeus vannamei*, underscoring the antioxidant and carotenoid potential of seed-derived matrices [6]. At the crop-biology level, genetics and seed-coat traits in *Cucurbita* spp. (*e.g.* white seed-coat phenotype regulated by MYB-linked pathways) intersect with phenylpropanoid/flavonoid metabolism, influencing phenolics, lignification and potentially extractable bioactives relevant to

oil/protein quality [7]. Complementary animal-nutrition studies also indicate PSO can enhance antioxidant capacity and immune markers under environmental stress, reinforcing its biofunctional profile [8]. Despite this progress, systematic profiling of the volatile and semi-volatile metabolome of white pumpkin seeds remains limited and few studies integrate chemical annotation with *in silico* pharmacokinetic (ADME) and toxicity (Tox) prediction to anticipate developability. This study therefore (i) characterizes the methanolic seed extract of white pumpkin seed by GC-MS method, and (ii) evaluates drug-likeness and safety *via* ADME/Tox tools to prioritize compounds for downstream biological validation. The resulting dataset aims to bridge compositional chemistry with oral developability signals, guiding bioactivity-guided fractionation and future nutraceutical or phytopharmaceutical development [1,2].

EXPERIMENTAL

Preparation of extract: Mature seeds of *Benincasa hispida* (white pumpkin/ash gourd) were collected from the local markets in Chennai, India. Botanical identity was confirmed by a qualified taxonomist (Dr. K. Devanathan, Department of Botany, The American College, Madurai, India). Seeds were washed thoroughly with tap water and rinsed with distilled water to remove surface debris. Clean seeds were shade-dried at ambient temperature (28 ± 2 ºC) for 10 days and milled to a fine powder using a mechanical grinder. For maceration, 10 g of seed powder was mixed with 100 mL of analytical-grade methanol (1:10 w/v) in a conical flask, sealed and agitated at 37 ºC on a rotary shaker for 48 h. The mixture was filtered through Whatman No. 1 filter paper and the filtrate was concentrated under reduced pressure at 40 ºC using a rotary evaporator. The crude methanolic extract was stored at 4 ºC in Amber vials for GC-MS profiling and *in silico* analyses.

GC–MS analysis: The GC-MS was employed to characterize the methanolic extract of white pumpkin seed. Analyses were performed on a Shimadzu QP-2010 Ultra GC-MS equipped with a non-polar capillary column (TRX-5MS, 30 m × 0.25 mm i.d., 0.25 μm film). Helium served as the carrier gas at a constant flow of 1.21 mL min^{-1}. The oven program was: 60 ºC hold, ramp to 280 ºC at 10 ºC min^{-1}. Injection volume was 2 μL (appropriate mode), and electron ionization (EI) was set at 70 eV. Total run time was 60 min with a scan range of *m/z* 40-650. Mass spectra were recorded and tentatively identified by comparison with the Wiley spectral library. The relative percentage of each component was calculated from normalized peak area (average peak area/total peak area) and ancillary parameters (molecular ion, molecular formula and putative structure) were used to support class assignment of detected metabolites.

ADME/Tox analysis: Absorption, distribution, metabolism and excretion (ADME) and toxicity (Tox) properties of GC-MS identified compounds were predicted using the pkCSM-pharmacokinetics web server (http://structure.bioc.cam.ac.uk/pkcsm). Simplified molecular-input line-entry specification (SMILES) strings for each compound were submitted to pkCSM, which applies graph-based signatures trained on experimental data to estimate key pharmacokinetic and toxicity endpoints [9]. Where applicable, additional descriptors were recorded to aid compound triage for downstream studies.

RESULTS AND DISCUSSION

Extraction and identification of phytocompounds are the fundamental steps for ensuring the reliability and reproducibility of herbal formulations. In present study, GC-MS technique was employed to determine the chemical constituents of the methanolic seed extract of white pumpkin. The chromatogram revealed 21 retention peaks, corresponding to a spectrum of bioactive metabolites such as fatty acids, esters, phytosterols, terpenoids, alkanes and tocopherols (Fig. 1). The major constituents identified were 9,12-octadecadienoic acid, methyl ester (20.9 %) and γ-sitosterol (14%), along with palmitic acid, oleic acid and stigmasterol derivatives. These findings are consistent with the results of Muzahid *et al.* [1], who analyzed *B. hispida* and *Cucurbita moschata* seed extracts across multiple solvents and found 9,12-octadecadienoic acid (Z,Z) and *n*-hexadecanoic acid as dominant lipids, together accounting for more than 70% of total composition in methanolic fractions. Likewise, Hu *et al.* [10] and Šamec *et al.* [11] also confirmed that unsaturated fatty acids (linoleic and oleic acids), phytosterols and tocopherols constitute the principal bioactive groups responsible for the anti-inflammatory, antioxidant and hypolipidemic activities of pumpkin seed oils. The qualitative pattern of the methanolic extract aligns well with the lipid-dominant chemoprofile of cucurbit seeds reported earlier. In *B. hispida*, Muzahid *et al.* [1] observed that the relative abundance of linoleic acid varies with solvent polarity, *e.g.* methanol extracts yielding a higher proportion of PUFAs than non-polar solvents, while *n*-hexane extracts retained higher saturated lipid fractions. Similarly, the occurrence of γ-sitosterol and stigmasterol as secondary metabolites is consistent with the sterol fraction as observed by Abdelnour *et al.* [8] and Ren *et al.* [12], both of whom highlighted their relevance in improving lipid metabolism and conferring cardioprotective effects. Minor constituents such as methyl stearate, phytol, and tocopherol analogs detected in the present study also correspond to those identified in *C. pepo* and *C. moschata* seed oils analyzed by Tantawy *et al.* [3] and Zancan *et al.* [6], further validating the consistency of pumpkin seed metabolite profiles across species. The predominance of linoleic and oleic acid methyl esters indicates potential hypolipidemic and antioxidant roles, as these compounds modulate cholesterol metabolism and inhibit lipid peroxidation. Collectively, the GC-MS profile of white pumpkin seed extract obtained in this study corroborates the previous findings in related cucurbit species and provides a robust foundation for ADME/Tox-guided screening of its compounds as nutraceutical leads. Retention time, molecular formula, molecular weight, compound class and relative peak area are summarized in Table-1, offering a detailed chemical reference for future standardization and therapeutic exploration.

ADME/Tox analysis: The bioactive compounds identified by GC-MS analysis from the methanolic seed extract of white pumpkin were further evaluated for their pharmacokinetic and toxicity parameters using the pkCSM web server to predict absorption, distribution, metabolism, excretion, and toxicity (ADME/Tox) profiles. Each compound was analyzed against Lipinski's rule of five, which stipulates that a potential drug candidate should meet at least three of the following five conditions: molecular weight ≤ 500 g/mol, hydrogen bond

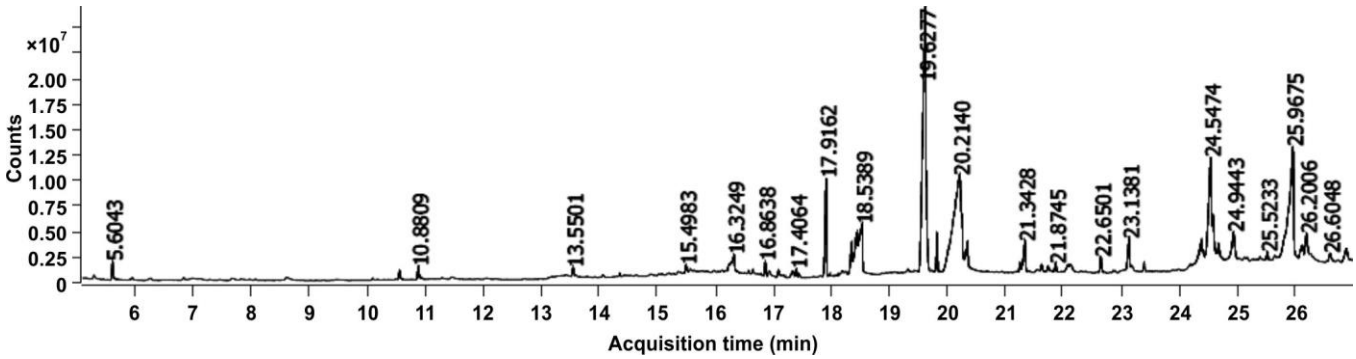

Fig. 1. GC-MS analysis of methanol extract of white pumpkin seed

TABLE-1
COMPOUND PRESENT IN METHANOL EXTRACT OF WHITE PUMPKIN SEED BY USING GS-MS ANALYSIS

Compd. No.	Compound name	Retention time (min)	Peak area (%)	m.f.	CAS number
1	9,12-Octadecadienoic acid (Z,Z)-, methyl ester	19.6277	20.90	$C_{19}H_{34}O_2$	112-63-0
2	γ-Sitosterol	25.9675	13.99	$C_{29}H_{50}O$	83-47-6
3	9,12-Octadecadienoic acid (Z,Z)-, 2,3-dihydroxypropyl ester	24.5474	7.70	$C_{21}H_{38}O_4$	2277-28-3
4	*n*-Hexadecanoic acid	18.5389	4.06	$C_{16}H_{32}O_2$	57-10-3
5	Hexadecanoic acid, methyl ester	17.9162	3.59	$C_{17}H_{34}O_2$	112-39-0
6	9,12,15-Octadecatrienoic acid, 2,3-dihydroxypropyl ester, (Z,Z,Z)-	24.5910	2.30	$C_{21}H_{36}O_4$	18465-99-1
7	*n*-Hexadecanoic acid	18.4369	2.07	$C_{16}H_{32}O_2$	57-10-3
8	Stigmasterol	24.9443	2.07	$C_{29}H_{48}O$	83-48-7
9	Tetradecanoic acid	16.3249	1.78	$C_{14}H_{28}O_2$	544-63-8
10	Campesterol	24.3908	1.77	$C_{28}H_{48}O$	474-62-4
11	Piperine	26.2006	1.76	$C_{17}H_{19}NO_3$	94-62-2
12	9-Octadecenoic acid, 12-hydroxy-, methyl ester, [R-(Z)]-	21.3428	1.60	$C_{19}H_{36}O_3$	141-24-2
13	Octadecanoic acid	20.3524	1.55	$C_{18}H_{36}O_2$	57-11-4
14	9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	20.2577	1.53	$C_{18}H_{30}O_2$	463-40-1
15	1,2-Benzenedicarboxylic acid, butyl octyl ester	18.3495	1.30	$C_{20}H_{30}O_4$	84-78-6
16	Octadecanoic acid, 2,3-dihydroxypropyl ester	24.6821	1.23	$C_{21}H_{42}O_4$	123-94-4
17	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	23.1381	1.22	$C_{19}H_{38}O_4$	23470-00-0
18	Stigmasta-5,24(28)-dien-3-ol, (3β,24Z)-	26.1241	1.19	$C_{29}H_{48}O$	481-14-1
19	*n*-Hexadecanoic acid	18.4551	1.14	$C_{16}H_{32}O_2$	57-10-3
20	Methyl stearate	19.8280	1.07	$C_{19}H_{38}O_2$	112-61-8
21	9,19-Cyclolanost-24-en-3-ol, (3β)-	26.8779	1.00	$C_{30}H_{50}O$	469-38-5

donors ≤ 5, hydrogen bond acceptors ≤ 10, log P ≤ 5 and molecular refractivity between 40 and 130. Among the 21 compounds evaluated, the majority complied with Lipinski's rule of five, indicating favourable potential for oral bioavailability (Table-2). Compounds such as 9,12-octadecadienoic acid (Z,Z)-, methyl ester, γ-sitosterol, stigmasterol and campesterol were found to exhibit favourable drug-like characteristics, comparable to findings from Muzahid *et al*. [1] and Hu *et al*. [10], who reported the similar compliance in pumpkin seed lipid extracts.

Water solubility and intestinal permeability are the key determinants for absorption. The pkCSM results revealed that most *B. hispida* compounds had high water solubility and good gastrointestinal (GI) absorption, particularly unsaturated fatty acid esters such as 9,12-octadecadienoic acid methyl ester and 9,12,15-octadecatrienoic acid esters, aligning with the reports of Šamec *et al*. [11], who identified linoleic and linolenic acid derivatives as highly permeable and bioavailable lipids. Compounds like γ-sitosterol and 9,19-cyclolanost-24-en-3-ol showed relatively low GI absorption, likely due to their high molecular weights and sterol backbone structure, which restrict passive diffusion across intestinal membranes. Distribution patterns were predicted by blood-brain barrier (BBB) permeability and volume of distribution (VDss). Compounds such as 9,12-octadecadienoic acid methyl ester, *n*-hexadecanoic acid and stigmasterol demonstrated potential to cross the BBB (log BB ≈ 0.30 – 0.40; Table-3), consistent with their lipophilicity and possible central activity. These observations are in line with Abdelnour *et al*. [8], who described pumpkin seed oil-derived fatty acids as BBB-permeable and potentially neuroprotective due to their ability to modulate oxidative stress and neuronal signalling.

Conversely, few compounds such as γ-sitosterol and campesterol showed limited BBB permeability, which may restrict central nervous system (CNS) exposure. Cytochrome P450 (CYP450) interactions revealed that several compounds, including 9,12-octadecadienoic acid methyl ester, γ-sitosterol and hexadecanoic acid methyl ester, were predicted to inhibit CYP3A4 and CYP2D6 isoenzymes. This profile suggests reasonable metabolic stability but indicates a need to evaluate potential drug–drug interactions when co-administered with

TABLE 2
PHARMACOPHORE PROPERTIES OF SELECTED COMPOUNDS FROM METHANOL EXTRACT OF WHITE PUMPKIN SEED

Compounds	Molecule properties					
	m.w. (g/mol)	Log P	#Rotatable bonds	#Acceptors	#Donors	Surface area (Å^2)
9,12-Octadecadienoic acid (Z,Z)-, methyl ester	533	6.7	16	2	0	26.3
γ-Sitosterol	292	8.6	6	1	1	20.2
9,12-Octadecadienoic acid (Z,Z)-, 2,3-dihydroxypropyl ester	533	5.2	17	3	2	60.0
n-Hexadecanoic acid	199	6.2	14	1	1	37.3
Hexadecanoic acid, methyl ester	493	6.6	15	2	0	26.3
9,12,15-Octadecatrienoic acid, 2,3-dihydroxypropyl ester, (Z,Z,Z)-	202	5.1	17	3	2	60.0
n-Hexadecanoic acid (2)	403	6.2	14	1	1	37.3
Stigmasterol	547	8.6	6	1	1	20.2
Tetradecanoic acid	581	5.6	12	1	1	37.3
Campesterol	583	8.0	5	1	1	20.2
Piperine	430	2.8	6	3	0	38.8
9-Octadecenoic acid, 12-hydroxy-, methyl ester, [R-(Z)]-	554	6.1	16	3	1	43.0
Octadecanoic acid	598	7.0	15	1	1	37.3
9,12,15-Octadecatrienoic acid, (Z,Z,Z)-	330	6.5	15	1	1	37.3
1,2-Benzenedicarboxylic acid, butyl octyl ester	466	7.2	15	4	0	52.6
Octadecanoic acid, 2,3-dihydroxypropyl ester	453	5.4	17	3	2	60.0
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	520	5.3	16	3	2	60.0
Stigmasta-5,24(28)-dien-3-ol, (3β,24Z)-	435	8.3	6	1	1	20.2
n-Hexadecanoic acid (3)	466	6.2	14	1	1	37.3
Methyl stearate	459	7.6	16	2	0	26.3
9,19-Cyclolanost-24-en-3-ol, (3β)-	545	8.5	5	1	1	20.2

TABLE-3
ABSORPTION AND DISTRIBUTION OF COMPOUNDS IDENTIFIED FROM GCMS ANALYSIS OF METHANOL EXTRACT OF WHITE PUMPKIN SEED

Compd. No.	Water solubility	Caco2 permeability	Intestinal absorption (human)	Skin permeability	P-glycoprotein			VDss (human)	Fraction unbound (human)	BBB permeability	CNS permeability
					P-gp substrate	P-gp I inhibitor	P-gp II inhibitor				
1	-2.036	1.206	91.324	-2.287	No	Yes	Yes	0.721	0.051	0.350	-1.769
2	-3.643	0.571	23.842	-2.384	No	Yes	Yes	0.684	0.051	-1.046	-3.526
3	-3.601	0.581	57.518	-2.364	No	No	Yes	0.286	0.206	-1.022	-3.555
4	-1.966	1.249	60.021	-2.207	No	No	Yes	0.734	0.052	-0.973	-3.544
5	-3.608	0.611	57.733	-2.272	No	Yes	No	0.687	0.202	-0.966	-3.512
6	-3.662	0.579	87.423	-2.212	No	No	No	0.668	0.207	-0.967	-3.402
7	-1.954	1.211	87.397	-2.274	No	No	No	0.709	0.049	-1.029	-3.467
8	-3.327	0.627	90.291	-2.214	No	No	No	0.706	0.052	0.340	-3.540
9	-3.357	0.578	93.997	-2.400	No	No	No	0.293	0.200	-1.039	-3.482
10	-1.989	0.609	90.275	-2.313	No	No	No	0.683	0.049	-0.994	-3.522
11	-1.934	1.147	92.951	-2.404	No	Yes	Yes	0.313	0.468	-1.025	-3.654
12	-2.042	1.159	90.437	-2.397	No	No	No	0.721	0.198	0.349	-1.816
13	-2.054	0.611	60.754	-2.372	No	Yes	No	0.669	0.051	-0.968	-3.438
14	-1.928	0.598	87.172	-2.341	No	No	No	0.666	0.050	-1.021	-3.663
15	-3.502	0.577	86.033	-2.342	No	No	No	0.289	0.210	-0.964	-3.396
16	-3.355	0.598	93.577	-2.222	No	No	No	0.702	0.207	0.340	-1.832
17	-4.928	0.617	91.232	-2.995	No	No	No	0.707	0.048	-0.976	-3.595
18	-4.859	0.579	86.969	-2.918	No	No	No	0.683	0.052	-1.017	-3.380
19	-3.482	0.583	89.927	-2.403	No	Yes	No	0.731	0.051	-1.041	-3.428
20	-3.345	0.627	60.595	-2.252	No	No	No	0.669	0.197	-0.981	-3.427
21	-3.509	0.207	25.012	-2.972	No	Yes	No	0.720	0.050	-1.024	-3.591

CYP substrates (Table-4). Previous studies have documented similar CYP inhibition patterns in sterol-rich extracts from Cucurbita pepo and *B. hispida*, reinforcing the metabolic reactivity of phytosterols in lipid fractions. Regarding excretion, most compounds demonstrated moderate to high renal and hepatic clearance (Table-4), reflecting balanced excretory profiles. The fatty acid methyl esters, due to their lipophilicity, are likely to be eliminated through hepatic metabolism rather than direct renal excretion, supporting the pharmacokinetic trend seen in edible seed oils as reported by Zancan *et al.* [6].

The toxicity evaluation (Table-5) indicated that most compounds were non-toxic, AMES-negative (non-mutagenic) and non-hepatotoxic, supporting their suitability for nutraceutical applications. However, octadecanoic acid and campesterol displayed mild hepatotoxic potential, which warrants further *in vitro* verification. 9,12-Octadecadienoic acid methyl ester and stigmasterol satisfied the key ADME/

TABLE-4
METABOLISM AND EXCRETION OF COMPOUNDS IDENTIFIED FROM GCMS ANALYSIS OF METHANOL EXTRACT OF WHITE PUMPKIN SEED

Compd. No.	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Total clearance (log mL/min/kg)	Renal OCT2 substrate
1	No	Yes	No	No	No	No	Yes	0.415	No
2	No	Yes	No	Yes	Yes	Yes	Yes	-0.091	No
3	No	Yes	No	No	No	No	Yes	0.444	No
4	No	No	No	No	Yes	No	No	0.544	No
5	No	Yes	No	No	No	No	Yes	0.479	No
6	No	Yes	No	No	No	No	Yes	0.429	No
7	No	No	No	No	Yes	No	No	0.598	No
8	No	Yes	No	Yes	Yes	Yes	Yes	-0.107	No
9	No	No	No	No	Yes	No	No	0.590	No
10	No	Yes	No	Yes	Yes	Yes	Yes	-0.097	No
11	Yes	Yes	Yes	No	No	No	No	0.286	No
12	No	Yes	No	No	No	No	Yes	0.488	No
13	No	No	No	No	Yes	No	No	0.523	No
14	No	No	No	No	Yes	No	No	0.529	No
15	No	Yes	No	Yes	No	No	No	0.379	No
16	No	Yes	No	No	No	No	Yes	0.424	No
17	No	Yes	No	No	No	No	Yes	0.481	No
18	No	Yes	No	Yes	Yes	Yes	Yes	-0.094	No
19	No	No	No	No	Yes	No	No	0.573	No
20	No	No	No	No	No	No	No	0.353	No
21	No	Yes	No	Yes	Yes	Yes	Yes	-0.102	No

TABLE-5
TOXICITY OF COMPOUNDS IDENTIFIED FROM GCMS ANALYSIS OF METHANOL EXTRACT OF WHITE PUMPKIN SEED

Compd. No.	AMES toxicity	Maximum tolerated dose (human) [log mg/kg/day]	hERG I inhibitor	hERG II inhibitor	Oral rat acute toxicity (LD_{50}) [mol/kg]	Oral rat chronic toxicity (LOAEL) [log mg/kg_bw/day]	Hepato-toxicity	Skin sensiti-zation	*T. pyriformis* toxicity [log µg/mL]	Minnow toxicity [log mM]
1	No	0.417	No	Yes	4.399	0.748	No	No	-0.394	0.089
2	No	0.480	No	No	3.374	0.621	No	No	-0.216	-0.201
3	No	0.466	No	No	3.343	0.379	No	No	-0.218	-0.190
4	No	0.478	No	No	3.120	0.842	No	No	-0.390	0.068
5	No	0.398	No	No	2.355	0.864	No	No	-0.118	0.063
6	No	0.429	No	No	2.870	0.463	No	No	-0.358	0.031
7	No	0.620	No	No	2.022	0.833	No	No	-0.141	-0.032
8	No	0.529	No	No	3.713	0.638	No	No	-0.364	-0.000
9	No	0.729	No	No	3.083	0.751	Yes	No	-0.391	-0.027
10	No	0.658	No	No	4.067	0.703	Yes	No	-0.377	-0.149
11	No	0.660	No	No	4.478	0.749	No	No	-0.131	-0.139
12	No	0.503	No	No	1.821	0.480	No	No	-0.333	-0.208
13	No	0.531	No	No	2.891	0.761	Yes	No	-0.111	-0.162
14	No	0.421	No	No	3.308	0.551	Yes	No	-0.128	-0.166
15	Yes	0.591	No	No	4.085	0.699	No	No	-0.290	-0.029
16	No	0.444	No	No	2.360	0.712	Yes	No	-0.197	-0.244
17	No	0.628	No	No	2.960	0.517	No	No	-0.298	-0.210
18	No	0.507	No	No	3.466	0.783	No	No	-0.372	0.064
19	No	0.377	No	No	4.491	0.879	No	No	-0.207	-0.221
20	No	0.577	Yes	No	3.791	0.827	Yes	No	-0.235	-0.008
21	No	0.638	No	No	4.039	0.557	No	No	-0.203	-0.051

Tox parameters and therefore represent promising leads for follow-up. These outcomes are in strong agreement with Ebrahimi *et al*. [4] and Morrison *et al*. [2], were reported that unsaturated fatty acids and phytosterols from pumpkin and related cucurbit seeds possess low toxicity and significant antioxidant potential.

Conclusion

The present study provides an integrated chemical and pharmacokinetic evaluation of the methanolic seed extract of *Benincasa hispida* (white pumpkin). The GC-MS profiling identified 21 bioactive compounds dominated by fatty-acid methyl esters and phytosterols, mainly 9,12-octadecadienoic acid, methyl ester and γ-sitosterol. *In silico* ADME/Tox prediction revealed that most compounds fulfilled Lipinski's criteria, exhibited high gastrointestinal absorption, moderate blood-brain-barrier permeability and minimal predicted toxicity. The fatty-acid esters showed favourable solubility and distribution characteristics, while the sterol derivatives demonstra-

ted metabolic stability with limited CYP450 inhibition. Toxicity parameters indicated non-mutagenic and non-hepatotoxic behaviour for the majority of constituents, underscoring their safety for nutraceutical application. Thus, the pharmacokinetic and safety profiles support the therapeutic potential of *B. hispida* seed bioactives as natural candidates for formulation development and future *in vitro* and *in vivo* validation.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

DECLARATION OF AI-ASSISTED TECHNOLOGIES

During the preparation of this manuscript, the authors used an AI-assisted tool(s) to improve the language. The authors reviewed and edited the content and take full responsibility for the published work.

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