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In-silico ADME Toxicity Analysis of Impurities in Commercially Marketed Δ8-THC Products for Potential Bio-medical Applications

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ABSTRACT

Background: Δ8-Tetrahydrocannabinol (Δ8-THC) is a psychoactive cannabinoid compound naturally occurring in the Cannabis sativa plant. The commercial Δ8-THC products are typically synthesized from cannabidiol (CBD), which may lead to the formation of various impurities. These impurities may contribute to unintended pharmacological or toxicological effects, highlighting the need for comprehensive safety assessment.

Purpose: This study aims to assess the pharmacokinetic and toxicity profiles of Δ8-THC and its structurally related impurities using in silico methods, thereby providing preliminary safety insights before in vitro or in vivo experimentation.

Method: In silico ADMET predictions were performed using the pkCSM web server.

Results: All analyzed compounds possess good membrane permeability and showed favorable values for intestinal absorption. The skin permeability values were within acceptable limits, with the exception of compound 10 (log Kp value -2.443). This suggests that compound 10 may have significantly reduced dermal permeability. All compounds were also predicted to exhibit high Caco-2 cell permeability. Compounds 3, 6, 7, 8, 9 (0.704, 0.542, 0.531, 0.531, 0.648), and 11 (0.227) showed relatively low VDss values. This could influence their duration of action and tissue-specific effects. All the compounds are unlikely to penetrate the blood-brain barrier (BBB), based on predicted log BB and CNS permeability indices. Our predictions indicate that impurities 6, 7, 8, 10, and 12 have the potential to inhibit the hERG channel, flagging them as possible cardiotoxic agents.

Conclusion: Δ8-THC and its structurally related impurities exhibited favorable absorption and distribution characteristics; variations in volume of distribution and dermal permeability, particularly for compound 10, may influence their pharmacological behavior. The predicted hERG inhibition by impurities 6, 7, 8, 10, and 12 raises potential cardiotoxicity concerns. Future work should include in vitro and in vivo validation of these predictions, as well as expansion to include additional impurities formed under various synthetic and storage conditions.

1. Introduction

Delta-8-tetrahydrocannabinol (Δ8-THC) is a psychoactive cannabinoid that has garnered significant attention in recent years due to its pharmacological similarities to Δ9-THC, the principal psychoactive component of *Cannabis sativa* (ElSohly *et al.,* 2017*)*. Although Δ8-THC is one of over 100 cannabinoids naturally produced by the cannabis plant, it is typically found in trace amounts. Consequently, most Δ8-THC used in commercial products is synthetically derived through the chemical transformation of hemp-derived cannabidiol, a process that has gained popularity due to its legal permissibility under certain regulatory frameworks. However, the synthesis of Δ8-THC from CBD is a complex chemical reaction that often leads to the formation of numerous by-products and structural isomers as impurities (Meehan-Atrash *et al.*, 2021; Thomas & Pollard, 2018). These impurities are seldom removed completely and may remain in final commercial products. Their presence has raised growing concerns regarding the toxicological safety and pharmacological effects of Δ8-THC formulations, especially as many of these products are marketed with limited quality control, regulatory oversight, or clinical evaluation.

As Δ8-THC-based products become more widespread, there is an urgent need for comprehensive toxicity profiling, not only of the active pharmaceutical ingredient (API), but also of its associated impurities (Poklis *et al.*, 2022; Snyder *et al.*, 2001). The toxicity of a drug product is frequently influenced by structurally related impurities, some of which may be genotoxic, carcinogenic, or cardiotoxic (Jamei *et al.*, 2019; Li, 2001; Van de Waterbeemd & Gifford, 2003). Recognizing this, several international regulatory authorities, including the U.S. FDA, EMA, and ICH, have established guidelines for the identification, quantification, and control of impurities in both pharmaceutical substances and finished products. In particular, the control of genotoxic and structurally alerting impurities has become a key concern in preclinical safety assessment (Gleeson *et al.,* 2011*)*. One of the most promising approaches for early-stage toxicity evaluation is the use of in silico predictive models, which enable researchers to estimate ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties of chemical compounds using computational tools (Pires *et al.*, 2015; Ekins *et al.*, 2017). Among these, the pkCSM platform (Mohammad *et al.*, 2023) has proven effective for predicting pharmacokinetic and toxicological endpoints based on graph-based molecular signatures. Such models allow for cost-effective, rapid screening of numerous compounds, providing valuable insights into their biological behavior prior to empirical testing (Radwan *et al.*, 2023).

In this study, we perform an in silico ADMET and toxicity evaluation of Δ8-THC and eleven structurally related impurities, designated as compounds 1 through 12, respectively (Figure 1). These impurities were previously isolated and structurally characterized using a combination of chromatographic and spectroscopic techniques (Radwan *et al.*, 2023). Their structures include a variety of Δ8-THC isomers, hydroxylated and epoxidized derivatives, and known cannabinoids such as Δ9-THC and cannabicitran. The structural diversity of these compounds offers an excellent framework for exploring structure–toxicity relationships (STRs) and understanding how minor changes in molecular configuration influence pharmacokinetic behavior and toxicity profiles (pkCSM, n.d.).Through this analysis, we aim to contribute to the improvement of drug quality control standards for cannabinoid-based therapeutics and to support regulatory science by identifying potentially harmful compounds within Δ8-THC formulations. The outcomes of this study can also be extended to guide the evaluation of impurities in other synthetically derived phytochemicals.

2. Materials and Methods

2.1. Overview of Computational Approach

Computer-Aided Drug Design (CADD) has emerged as a powerful approach in modern drug discovery and toxicity prediction. Compared to traditional experimental techniques, CADD enables high-throughput screening of chemical entities with significantly reduced time, cost, and resource requirements. In particular, in silico prediction of pharmacokinetic properties such as absorption, distribution, metabolism, excretion, and toxicity (ADMET) plays a pivotal role in identifying promising lead compounds and eliminating potentially harmful candidates early in the development pipeline (Zhang *et al.*, 2025).

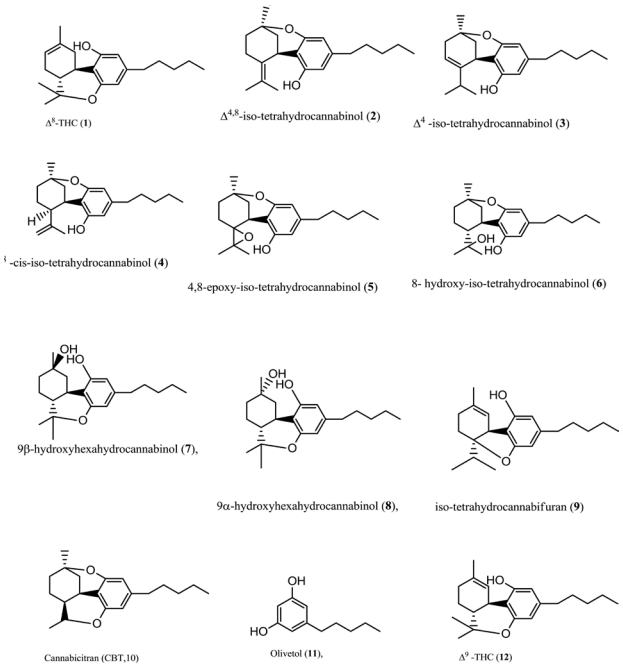

Figure 1: Chemical Structures of Δ^8-THC (1) And Structurally Related Impurities (2-12) Identified in Commercial Cannabinoid Products

2.2. Selection of Compounds

A total of twelve chemical compounds were selected for this study, comprising Δ8-tetrahydrocannabinol (Δ8-THC) as the reference compound (compound 1) and eleven associated impurities (compounds 2-12), previously isolated and characterized. These impurities include various isomers and degradation products of Δ8-THC, such as Δ4,8-iso-THC, Δ9-THC, o-olivetol, and hydroxylated or epoxidized derivatives. The chemical structures of these compounds were retrieved or drawn manually using cheminformatics software and optimized prior to ADMET evaluation (Radwan *et al.*, 2023).

2.3. Molecular Descriptor Considerations

The pharmacokinetic behavior of small molecules is governed by several key physicochemical properties. The

Lipinski Rule of Five (Lipinski, 2004), a widely used drug-likeness filter, states that orally active drugs are more likely to meet the following criteria: molecular weight (MWT) ≤ 500 Da, LogP (octanol-water partition coefficient) ≤ 5, number of hydrogen bond donors ≤ 5, and number of hydrogen bond acceptors ≤ 10. These parameters are closely associated with aqueous solubility, intestinal permeability, and oral bioavailability. Additional molecular descriptors, such as topological polar surface area (TPSA), number of rotatable bonds, and skin permeability, are also crucial in evaluating a compound's ability to cross biological membranes and interact with metabolic enzymes or receptors.

2.4. ADMET Prediction using pkCSM

The pkCSM web server (http://biosig.unimelb.edu.au/pkcsm/) was used to predict ADMET profiles of the selected compounds. pkCSM employs a graph-based machine learning approach to estimate over 25 pharmacokinetic and toxicity-related endpoints using molecular structure as input. The SMILES (Simplified Molecular Input Line Entry System) representations of each compound were uploaded to the pkCSM server, and the following parameters were assessed: Absorption: water solubility (log S), Caco-2 permeability, human intestinal absorption (HIA), skin permeability (log Kp), and P-glycoprotein substrate/inhibitor prediction. Distribution: volume of distribution at steady state (VDss), blood–brain barrier (BBB) permeability, and central nervous system (CNS) permeability. Metabolism: interaction with cytochrome P450 (CYP) enzymes, including CYP3A4 and CYP2D6 substrates/inhibitors. Excretion: total clearance and renal OCT2 substrate status. Toxicity: Ames mutagenicity, hERG I/II inhibition (cardiotoxicity), hepatotoxicity, and skin sensitization. The results were exported and analyzed to identify key pharmacokinetic risks or potential liabilities among the tested impurities.

2.5. Rationale for In-Silico Evaluation

The use of in silico tools such as pkCSM enables rapid screening of candidate molecules and associated impurities without the need for extensive laboratory testing. This approach provides an early estimation of the drug-likeness, toxicity, and safety profile of unknown or novel compounds. In the context of Δ8-THC and its manufacturing by-products, such predictions are essential for guiding regulatory assessment, ensuring consumer safety, and enhancing product quality control standards.

3. Results and Discussion

Physicochemical, pharmacokinetic (ADME), metabolic, and toxicological properties of Δ8-THC (Compound 1) and its structurally related impurities (Compounds 2-12) were evaluated using the pkCSM in silico model to predict their drug-likeness, absorption, distribution, metabolism, excretion, and potential toxicological risks. The ADMET properties of Δ8-THC and its eleven known impurities were predicted using the pkCSM web server. These in silico evaluations provide insights into the pharmacokinetic and toxicity profiles of the compounds, which are essential for assessing their potential safety and bioavailability (Gallardo *et al*., 2024). Below, we present a detailed analysis of each ADMET parameter.

3.1. Physicochemical Properties

The physicochemical properties of Δ8-THC (Compound 1) and its structurally related impurities (Compounds 2-12), as predicted by pkCSM and summarized in Table 1. All twelve compounds exhibited molecular weights below 500 Da, satisfying one of the criteria of the Lipinski Rule of Five, which predicts good oral bioavailability. Lower molecular weight generally enhances membrane diffusion, cellular transport, and solubility. As molecular weight increases, steric bulk and molecular volume also increase, often reducing permeability and transport efficiency. The hydrogen bond donor (HBD) and acceptor (HBA) counts were within acceptable ranges for all compounds, with HBDs ranging from 0 to 2 (≤5) and HBAs ranging from 2 to 3 (≤10). These values suggest that the compounds are capable of forming hydrogen bonds while still maintaining suitable membrane permeability. Topological polar surface area (TPSA) was another key indicator analyzed. Most compounds displayed TPSA values exceeding 140 Å², indicative of relatively high polarity. Notably, compounds 10 (Olivetol) and 11 (Δ9-THC) had lower TPSA values, suggesting better membrane absorption and increased oral bioavailability compared to the more polar compounds.

In general, compounds with TPSA > 140 Å² may face absorption challenges through biological membranes. The number of rotatable bonds is indicative of molecular flexibility, which contributes to favorable binding interactions in biological targets (Al-Azzam, 2022). All compounds were within acceptable flexibility ranges. In particular, flexible molecules often exhibit better adaptability to enzyme and receptor binding sites. AlogP values were used to estimate lipophilicity. Compounds 6, 7, 8, and 11 exhibited ideal lipophilicity with AlogP ≤ 5, aligning with known favorable membrane interactions. However, the remaining compounds showed higher AlogP values (>5), which may suggest poor aqueous solubility and increased risk of nonspecific binding or toxicity. An optimal balance between hydrophilicity and lipophilicity is crucial for ensuring proper absorption, distribution, and clearance.

Table 1: Physicochemical Properties of Δ^8-THC (Compound 1) and Structurally Related Impurities (Compounds 2–12) Predicted by pkCSM

Compound No.	Molecular Formula	M.W	HBD	HBA	nrotb	Log P	Surface area
1	$C_{11}H_{16}O_2$	314.46	1	2	4	5.7358	140.112
2	$C_{21}H_{30}O_2$	314.46	1	2	4	5.8799	140.112
3	$C_{20}H_{28}O_2$	314.469	1	2	5	5.7358	140.112
4	$C_{21}H_{30}O_2$	314.469	0	2	5	5.7358	140.112
5	$C_{21}H_{30}O_3$	330.468	1	3	4	5.0911	144.909
6	$C_{21}H_{32}O_3$	332.484	2	3	5	4.9306	145.596
7	$C_{21}H_{32}O_3$	332.484	2	3	4	4.9306	145.596
8	$C_{21}H_{32}O_3$	332.484	2	3	4	4.9306	145.596
9	$C_{21}H_{30}O_2$	314.469	1	2	5	5.7358	140.112
10	$C_{20}H_{28}O_2$	300.442	0	2	4	5.235	133.75
11	$C_{11}H_{16}O_2$	180.247	2	2	4	2.8305	78.845
12	$C_{21}H_{30}O_2$	314.469	1	2	4	5.7358	140.112

3.2. Absorption

The absorption parameters (Table 2) considered include Caco-2 permeability, human intestinal absorption, skin permeability (log Kp), and P-glycoprotein (P-gp) interaction. All compounds demonstrated high predicted Caco-2 permeability (Papp > 0.90), indicating strong potential for passive intestinal absorption. Human intestinal absorption (HIA) for all compounds was also predicted to be above 30%, confirming good oral absorption across the series. Skin permeability (log Kp) values were generally acceptable (> -2.5), except for compound 10, which showed reduced skin permeability (log Kp = -2.443). This suggests that most compounds can be absorbed through the skin, potentially relevant in transdermal formulations or accidental exposure. P-glycoprotein plays a crucial role in drug efflux and can impact oral bioavailability and blood-brain barrier permeability. Interestingly, all tested compounds were predicted to be P-gp substrates, indicating a likelihood of active efflux from cells. This may reduce intracellular accumulation and influence therapeutic efficacy, particularly in CNS or cancer-related applications (Domański *et al.*, 2023).

Table 2: Absorption Properties of the Selected Compounds

	Compound no	Water solubility (log mol/L)	Caco2 permeability (log Papp in 10^{-6} cm/s)	Intestinal absorption (human)% (Absorbed)	Skin Permeability (log Kp)	p-glycoprotein substrate	p-glycoprotein I inhibitor	p-glycoprotein II inhibitor
Absorption	**1**	-5.552	1.057	93.6	-2.814	No	Yes	No
	2	-5.801	1.275	92.813	-2.765	No	Yes	No
	3	-5.754	1.158	92.629	-2.765	Yes	No	No
	4	-5.59	1.151	92.755	-2.778	Yes	No	No

Absorption	**5**	-4.977	1.275	92.902	-3.243	Yes	Yes	No
	6	-4.045	1.414	92.501	-3.085	Yes	No	No
	7	-4.811	1.377	92.656	-3.504	Yes	Yes	No
	8	-4.811	1.377	92.656	-3.504	Yes	Yes	No
	9	-5.385	1.012	91.515	-2.643	Yes	Yes	No
	10	-5.778	1.167	95.788	-2.443	No	Yes	No
	11	-2.735	1.132	-	-2.899	Yes	No	No
	12	-5.673	1.146	93.176	-2.581	No	Yes	No

3.3. Distribution

The steady-state volume of distribution (VDss) helps estimate how widely a drug diffuses into body tissues. Table 3 presents the distribution properties of the selected compounds. Based on the predictions, Compounds 3, 6, 7, 8, 9, and 11 exhibited low VDss values (< 0.71 L/kg), suggesting that they are more likely to remain confined to the blood plasma and may have shorter half-lives. Other compounds showed moderate to high VDss values, indicating broader tissue distribution, which could impact both efficacy and toxicity. Blood–brain barrier permeability (logBB) and CNS permeability (logPS) were also predicted: Compounds 5-9 and 11 had logBB < 0.3, suggesting limited ability to cross the blood–brain barrier (BBB). In contrast, the other compounds may potentially penetrate the CNS. However, all compounds, including Δ8-THC, showed logPS < -3, indicating limited CNS permeability. This suggests that while some molecules may reach the brain, they may not readily cross into central compartments at pharmacologically significant levels, potentially due to P-gp efflux or limited lipophilicity (Onyango *et al.*, 2024).

Table 3: Distribution Properties of the Selected Compounds

	Compound No.	VDss (human) (log L/kg)	Fraction unbound (human)(Fu)	BBB permeability (log BB)	CNS permeability (log PS)
Distribution	**1**	0.798	0	0.387	-1.703
	2	0.818	0	0.375	-1.693
	3	0.704	0	0.508	-1.268
	4	0.795	0.002	0.467	-1.585
	5	0.717	0.049	-0.077	-2.038
	6	0.542	0.038	-0.233	-1.834
	7	0.531	0.058	-0.212	-1.784
	8	0.531	0.058	-0.212	-1.784
	9	0.648	0	0.711	-1.725
	10	0.894	0	0.488	-2.14
	11	0.227	0.354	0.17	-1.685
	12	0.864	0.02	0.569	-2.118

3.4. Metabolism

Metabolic prediction (Table 4) focused on interactions with cytochrome P450 enzymes, particularly CYP2D6 and CYP3A4, which are responsible for the metabolism of most clinical drugs. The findings indicated moderate interaction across the series, without strong inhibition or induction patterns. Total drug clearance, which reflects the rate of elimination, was highest for compound 4, suggesting a faster systemic removal compared to other impurities. Clearance is often influenced by hydrophilicity, metabolic stability, and molecular weight (Zanger & Schwab, 2023).

Table 4: Metabolism Properties of Δ^8-THC (Compound 1) and Structurally Related Impurities (Compounds 2–12) Predicted by pkCSM

	Compound No.	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitior	CYP2C19 inhibitior	CYP2C9 inhibitior	CYP2D6 inhibitior	CYP3A4 inhibitior
	1	No	Yes	Yes	Yes	No	No	Yes

Metabolism	**2**	No	Yes	Yes	Yes	No	No	Yes
	3	No	Yes	Yes	No	No	No	No
	4	No	Yes	Yes	Yes	No	No	No
	5	No	Yes	No	Yes	No	No	No
	6	No	Yes	No	No	No	No	No
	7	No	Yes	Yes	Yes	No	No	No
	8	No	Yes	Yes	No	No	No	No
	9	No	Yes	Yes	Yes	No	No	Yes
	10	No	Yes	No	Yes	No	No	No
	11	No	No	Yes	No	Yes	No	Yes
	12	No	Yes	Yes	Yes	No	No	No

3.5. Excretion

The predicted excretion profiles of Δ^8-THC (Compound **1**) and its structurally related impurities (Compounds 2-12), as presented in Table 5, demonstrate moderate to low total clearance values, ranging from 0.349 to 1.04 log ml/min/kg. Compound 4 exhibited the highest predicted clearance (1.04), suggesting a potentially faster elimination rate compared to the other compounds. In contrast, Compound 11 showed the lowest clearance (0.349), indicating a slower excretion rate. Notably, none of the compounds were identified as renal OCT2 substrates, implying that renal tubular secretion via OCT2 transporters may not play a significant role in their elimination. These findings contribute to a better understanding of the compounds' excretory behavior, which is essential for evaluating their pharmacokinetic and safety profiles (de Bruyn *et al.*, 2023).

Table 5: Predicted Excretion Properties of Δ^8-THC (Compound 1) and Structurally Related Impurities (Compounds 2-12) Predicted by pkCSM

	Compound No.	**Total Clearance (log ml/min/kg)**	**Renal OCT2 substrate**
Excretion	**1**	0.976	No
	2	0.974	No
	3	1	No
	4	1.04	No
	5	0.61	No
	6	0.899	No
	7	0.779	No
	8	0.779	No
	9	0.954	No
	10	0.959	No
	11	0.349	No
	12	0.888	No

3.6. Toxicity

Safety profiling using pkCSM included predictions for AMES toxicity, hepatotoxicity, hERG inhibition, and skin sensitization (Pires *et al.*, 2023).All compounds were predicted (Table 6) to be non-mutagenic in the AMES test and non-hepatotoxic, indicating general safety in terms of genotoxicity and liver toxicity. However, compounds 6, 7, 8, 10, and 12 were predicted to inhibit the hERG channel, suggesting a risk of cardiotoxicity (QT prolongation),

which is a major concern in drug development. These same compounds also showed potential for skin sensitization, raising concerns about dermal exposure or allergic reactions in topical applications.

Table 6: Predicted Toxicity Properties of Δ^8-THC (Compound 1) and Structurally Related Impurities (Compounds 2–12) Predicted by pkCSM

	Compound No.	AMES toxicity	Max. tolerated dose (human) (log mg/kg/day)	hERG I inhibitor	hERG II inhibitor	Oral Rat Acute Toxicity (LD50) (mol/kg)	Oral Rat Chronic Toxicity (LOAEL) (log mg/kg_bw/day)	Hepatotoxicity	Skin Sensitisation	T.Pyriformis toxicity (log ug/L)	Minnow toxicity (log mM)
Toxicity	**1**	No	-0.154	No	No	2.418	2.529	No	No	1.961	-1.101
	2	No	-0.331	No	No	2.41	2.463	No	No	2.109	-1.077
	3	No	-0.3	No	No	2.305	2.589	No	No	1.972	-1.226
	4	No	-0.199	No	No	2.334	2.493	No	No	2.083	-1.019
	5	No	-0.642	No	No	1.949	2.115	No	No	1.151	-0.684
	6	No	-0.692	No	Yes	2.733	2.269	No	No	1.01	0.17
	7	No	-0.247	No	Yes	2.411	1.857	No	No	1.625	0.287
	8	No	-0.247	No	Yes	2.411	1.857	No	No	1.625	0.287
	9	No	0.169	No	No	2.341	2.248	No	No	1.372	-0.954
	10	No	0.316	No	Yes	1.919	2.198	No	No	1.652	-0.814
	11	No	0.457	No	No	1.972	2.56	No	Yes	1.777	0.377
	12	No	0.309	No	Yes	2.176	2.185	No	No	2.134	-0.933

3.7. General Observations

The results indicate that most Δ8-THC-related impurities exhibit similar pharmacokinetic behaviors to the parent compound in terms of absorption and distribution, but certain derivatives pose greater toxicity risks, especially with respect to hERG inhibition and skin sensitization. Notably, compound 10 (Olivetol) displayed poor skin permeability but otherwise favorable ADMET features. Given the widespread and often unregulated use of Δ8-THC products, the presence of these impurities—even in trace quantities—warrants attention. This in silico assessment provides a rapid and cost-effective screening method to support drug quality control, regulatory decision-making, and public health protection (Franco *et al.*, 2023).

4. Conclusion and Future Directions

In this study, we performed a comprehensive in silico ADMET and toxicity analysis of Δ8-tetrahydrocannabinol (Δ8-THC) and eleven structurally characterized impurities commonly found in commercial Δ8-THC products. Using the pkCSM computational platform, we evaluated key pharmacokinetic parameters—including absorption, distribution, metabolism, excretion, and toxicity—to better understand the behavior and potential risks associated with these compounds. The results indicated that all compounds conformed to major drug-likeness criteria, such as molecular weight, hydrogen bonding potential, and membrane permeability. Most compounds demonstrated good oral absorption and favorable intestinal permeability, although some displayed elevated lipophilicity and polarity that could affect solubility and tissue distribution. P-glycoprotein substrate predictions suggest active efflux in vivo, which may influence bioavailability and therapeutic efficacy. Importantly, while the majority of compounds appeared non-mutagenic and non-hepatotoxic, a subset—including compounds 6, 7, 8, 10, and 12—exhibited potential cardiotoxicity via hERG channel inhibition and possible skin sensitization. These findings emphasize the need for impurity-specific safety evaluations, especially given the unregulated or semi-regulated sale of Δ8-THC products in several markets. The similarity in pharmacokinetic profiles between Δ8-THC and its impurities suggests that some toxic effects observed in clinical or user settings may be attributable not only to the active ingredient but also to co-existing synthetic by-products. This study highlights the value of in silico modeling as a first-line approach for early-phase

toxicity prediction and pharmacokinetic screening of both active pharmaceutical ingredients and their impurities. Such evaluations can significantly improve drug quality control, reduce downstream safety risks, and guide regulatory agencies in setting impurity limits for cannabinoid-based therapeutics.

While our computational findings provide strong predictive insights, further work is needed to validate these results: In vitro studies should be performed to confirm ADMET profiles, especially hERG inhibition, skin sensitization, and P-gp interactions. In vivo pharmacokinetic and toxicological studies are recommended to quantify systemic exposure and evaluate organ-specific toxicity of key impurities. Mechanistic docking and molecular dynamics simulations may offer deeper insight into target-specific interactions and toxicity pathways. Lastly, similar studies should be extended to other cannabinoids and synthetic derivatives, as the market continues to evolve with new compounds of unknown safety profiles. Overall, this study contributes to the scientific foundation required for the safe development, manufacturing, and regulation of cannabinoid-containing products.

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Authorship Contribution

Munagala Alivelu: Conceptualization, data collection, writing, and editing, and NatteKavitha: Conceptualization, write-up, and editing.

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Ethical Approvals

No ethical approvals were required for this study.

Declarations

The authors declare that they have followed all ethical standards in conducting this research. All data supporting the findings are available within the manuscript

Conflict of Interest

The authors declare no conflict of interest related to this study.

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