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Comparative computational study of the toxicological profile of a few avocado (*Persea americana* Mill) and papaya (*Carica papaya*) compounds used in the formulation of sunscreens

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ABSTRACT

Introduction
Exposure to ultraviolet (UV) radiation is inevitable and can lead to a range of skin damage and related illnesses. Sunscreens are commonly used to mitigate the harmful effects of UV radiation. However, many sunscreens contain synthetic compounds that are toxic and associated with various side effects. In response, natural alternatives, such as plant-based sunscreens, are gaining popularity. Additionally, several countries have banned animal testing for cosmetics, fostering the need for alternative testing methods like *in vitro* assays and computer models.

Purpose
This study aims to evaluate the toxicological profiles of eight compounds with photoprotective properties, including four from avocado and four from papaya, using computational methods.

Methods
We employed computer-based tools—SwissADME, pkCSM, and ADMETlab 3.0—to assess the bioavailability and establish the toxicological profiles of the selected compounds. These computational methods help reduce animal testing, aligning with ethical guidelines and animal welfare regulations.

Results
The analysis focused on the physicochemical, pharmacokinetic, and toxicological properties of the compounds, including the relationship between these properties and toxicity based on Pfizer and GSK rules. The bioavailability data indicated that none of the eight compounds fully met the optimal zone criteria. Among avocado-derived compounds, 2A showed the best bioavailability, while compound 1P from papaya exhibited the highest bioavailability. Toxicological findings revealed that compound 4P was likely carcinogenic, compound 2A was mutagenic, and compounds 4A and 3P were identified as eye irritants.

Conclusion
While there is growing interest in plant-based sunscreen ingredients such as avocado and papaya extracts, some of these compounds may still present toxicological risks. The study identified certain avocado and papaya compounds that could pose toxicity concerns, potentially limiting their effectiveness in sunscreen formulations. Given the preliminary nature of the findings from computer models, further experimental *in vitro* studies on the toxicity of these compounds are recommended.

INTRODUCTION

The sun has played a major role in human evolution, migration, and the diversity of our biological characteristics. An important part of this history is the skin, which protects us from external aggressors and regulates body temperature. The skin, our largest organ, weighing around 3 kilograms, is the most visible part of the body and reflects our relationship with the sun, influencing our identity and, at times, contributing to racial prejudice (Alain, 2012).

One of the components of sunlight is ultraviolet (UV) radiation, which is divided into UVA, UVB, and UVC. UV radiation is biologically active, but only UVA and UVB reach the skin (Bédane & Roelandts, 2007). The skin can reflect, diffract, transmit, or absorb this radiation, thereby influencing biochemical reactions within cells. It has been reported that UV radiation can be highly harmful to the skin and general health (Hamouda et al., 2015). It can cause burns, premature skin ageing, eye damage, immune system weakening, allergic reactions, and, in the most severe cases, various types of skin cancer—including melanoma, the most dangerous form (Hamouda et al., 2015).

Photoprotection refers to all strategies and interventions aimed at mitigating skin damage induced by solar radiation (D'Orazio, 2013; Grether-Beck et al., 2014). These strategies include the use of sunscreens, protective clothing, and hats. Sunscreens have become common in many cosmetic products as a means of protecting the skin from UV-induced ageing and damage. However, despite their effectiveness, some sunscreens can provoke allergic reactions and other dermatological issues (Geoffrey, 2019). Several studies have shown that some synthetic sunscreens are toxic, may have adverse effects on fertility, and are therefore increasingly being replaced or supplemented with plant-based alternatives (Mbanga et al., 2023; Yan et al., 2020).

Although natural plant-based products are popular for their efficacy and low toxicity, it is essential to recall Paracelsus' famous axiom: "*The dose makes the poison,*" which emphasises that any compound can become toxic once a certain concentration threshold is exceeded.

Over the last two decades, scientific research has been significantly transformed by technological advances, particularly in internet access and artificial intelligence (Isamura et al., 2023; Matondo et al., 2022; Mpiana et al., 2020; Yang et al., 2019). Improvements in computer hardware and algorithms have greatly expanded access to information, broadening the scope of research possibilities (Eissa et al., 2014; Lukuzu et al., 2024; Matondo et al., 2021; Mfutu et al., 2024; Ngbolua et al., 2022). Today, many researchers view computer simulations as being just as valid as laboratory experiments.

Moreover, ***in vivo*** studies—particularly those involving animals—are known to be time-consuming, costly, and increasingly considered unethical by the public. As a result, such testing has been banned under the new European Union cosmetics regulation (Regulation (EC) No. 1223/2009), which applies across all EU countries (CosmeticObs, 2019).

This regulation introduced strict measures encouraging the use of alternative testing methods. Other countries, including New Zealand and Argentina, have also enacted bans on animal testing in cosmetics. This global trend has led to a surge in the use of alternative approaches such as *in vitro* tests, computer models, and other innovative tools to assess the safety and efficacy of products without resorting to animal testing (Dent et al., 2018; Matthews, 2019). These alternatives are not only more ethical but can also be faster and more cost-effective—benefits highly valued in the cosmetics industry. In this context, many researchers are increasingly adopting in silico approaches to evaluate the safety of cosmetic-related substances, most of which are synthetic (Gellatly & Sewell, 2019; Taylor & Alvarez, 2020; Tcheremenskaia et al., 2019).

To the best of our knowledge, few studies have assessed the safety of natural cosmetic ingredients and products (Mulombela et al., 2024; Raitano et al., 2019). Furthermore, Raitano and colleagues, in their study on the safety of various natural cosmetic products, predicted only one toxicity descriptor—mutagenicity (Raitano et al., 2019).

In the present study, we report the toxicological profile of selected compounds using multiple descriptors, including eye irritation and eye corrosion. These compounds were isolated from avocado (*Persea americana* Mill.) and papaya

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(*Carica papaya*) (Figure 1), both of which are commonly used in sunscreen formulations due to their antioxidant properties (Alkaltham et al., 2021; Zunjar et al., 2015). This research is part of a broader project aimed at evaluating the toxicological profiles of natural products derived from plants and fruits used in sunscreen formulations (Mulombela et al., 2024).

Figure 1:
Avocado (*Persea americana* Mill.) and papaya (*Carica papaya*)

Among the compounds with antioxidant properties used in sunscreen formulations, we selected four from avocado, labelled 1A, 2A, 3A, and 4A (Figure 2), and four from papaya, labelled 1P, 2P, 3P, and 4P (Figure 3).

Figure 2:
Chemical structures of four isolated compounds from *Persea americana* Mill

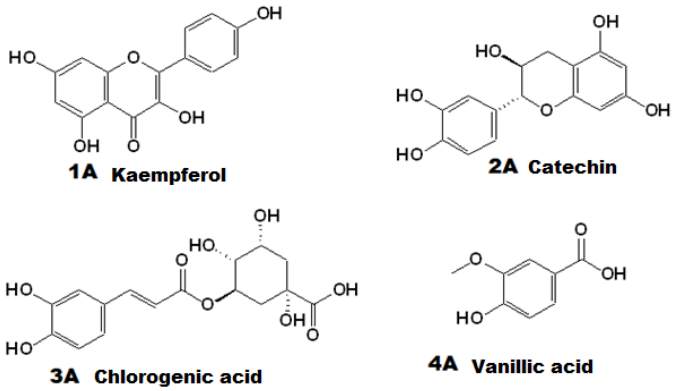
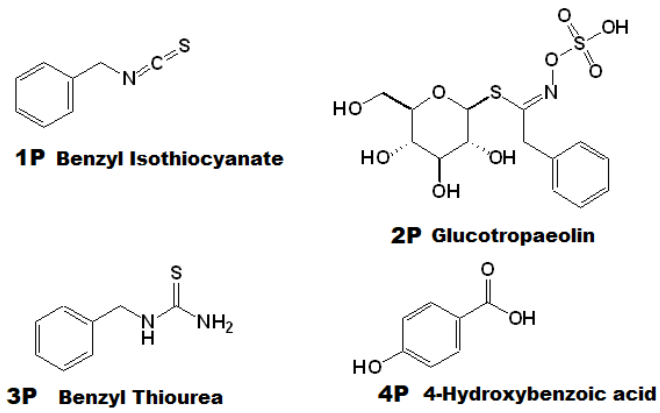


Figure 3:
Chemical structures of four isolated compounds from *Carica papaya*



METHODS

Studying the path taken by a compound—whether of natural or synthetic origin—is of paramount importance for understanding its behaviour in the body. This includes its entry into the body, whether by ingestion, inhalation, skin contact, or other means, through to its elimination. This process involves absorption, distribution, metabolism, and excretion, collectively referred to as ADME. Compounds used in cosmetic applications require in-depth evaluation of their physicochemical and pharmacokinetic properties (ADME) to ensure their efficacy, mode of action, and, most importantly, their safety. The latter involves toxicology, or more precisely, toxicological profiling.

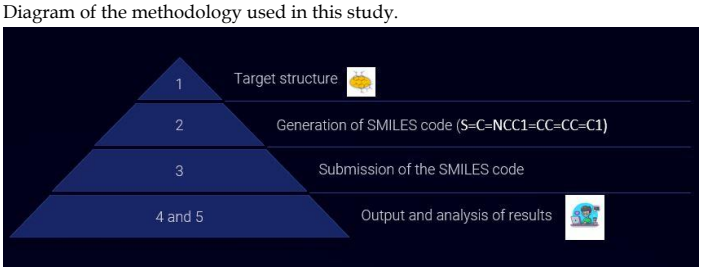
All these properties were predicted using computer models via web-based tools: SwissADME (Daina et al., 2017), pkCSM (Pires et al., 2015), and ADMETlab 3.0 (Fu et al., 2024). Although the effectiveness of these tools has already been demonstrated, we further evaluated their predictive performance by testing their ability to reproduce experimental results using *octocrylene*, a synthetic sunscreen known for its mutagenic and carcinogenic potential (Yan et al., 2020). The toxicological results for octocrylene were successfully replicated by all three software tools mentioned.

In addition to using an HP laptop for the simulations, the CambridgeSoft ChemDraw 2D and 3D Professional chemical editor was employed to construct the molecules, represent their chemical structures, and generate SMILES notations for all the investigated compounds (Weininger, 1998). SMILES (Simplified Molecular Input Line Entry System) codes enable the conversion of complex chemical structures into character strings that are easily manipulated by computational tools.

The methodology used in this study is summarised in five steps (see Figure 4):

1. Definition of the target structure;
2. Generation of the SMILES code (input);
3. Submission of the SMILES code to the software;
4. Retrieval of results (output);
5. Analysis of physicochemical parameters and toxicological profiles.

Figure 4:
Diagram of the methodology used in this study.



It is essential to interpret the values of physicochemical parameters in relation to the compound's biological activity and bioavailability. Evaluating the toxicological profile helps identify potential risks and target organs.

In silico approaches for predicting the toxicological profiles of compounds are powerful and widely adopted tools for assessing chemical safety. However, their limitations lie primarily in their capacity to replicate the biological complexity and multifaceted interactions that occur within living organisms.

RESULTS AND DISCUSSION

The selected compounds, illustrated in **Figures 2** and **3**, were converted to SMILES codes using the SwissADME software. Their respective SMILES codes and IUPAC names are presented in **Table 1**.

Table 1:
Canonical SMILES of the Investigated Compounds

No.	IUPAC Name	Canonical SMILES
1A	3,5,7-trihydroxy-2-(4-hydroxyphenyl)chromen-4-one	OC1=CC=C(C=C1)C1=C(O)C(=O)C2=C(O1)C=C(O)C=C2O
2A	(2S,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromen-3,5,7-triol	OC1CC2=C(OC1C1=CC=C(O)C(O)=C1)C=C(O)C=C2O
3A	3-[[3-(3,4-dihydroxyphenyl)-1-oxo-2-propenyl]oxy]-1,4,5-trihydroxycyclohexanecarboxylic acid	OC1CC(O)(CC(OC(=O)\C=C\C2=CC=C(O)C(O)=C2)C1O)C(O)=O
4A	4-Hydroxy-3-methoxybenzoic acid	COC1=CC(=CC=C1O)C(O)=O
1P	Benzyl isothiocyanate	S=C=NCC1=CC=CC=C1
2P	[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl] (1Z)-2-phenyl-N-sulfooxyethanimidothioate	OCC1OC(S\C(CC2=CC=CC=C2)=N/OS(O)(=O)=O)C@HC(O)[C@@H]1O
3P	Benzylthiourea	NC(=S)NCC1=CC=CC=C1
4P	Hydroxybenzoic acid	OC(=O)C1=CC=C(O)C=C1

Physico-chemical Parameter Analysis

The SMILES codes representing the chemical structures of the selected compounds were used as input for three software packages. Initially, the physico-chemical properties of the compounds were evaluated, as these characteristics provide essential insights into a molecule's chemical reactivity. In cosmetic formulations, these parameters influence product stability, texture, and skin penetration. In pharmacological contexts, they are critical for predicting ADME (Absorption, Distribution, Metabolism, and Excretion) properties (Mvondo et al., 2021).

According to Lipinski's Rule of Five (Lipinski, 2000), a compound is likely to have good oral bioavailability if it meets the following criteria:

1. Molecular weight (MW) ≤ 500 Da
2. Hydrogen bond acceptors (nHA) ≤ 10
3. Hydrogen bond donors (nHD) ≤ 5
4. Log P ≤ 5

The analysed parameters include molecular weight (MW, in g/mol), Log P (logarithm of the octanol-water partition coefficient), number of hydrogen bond acceptors (nHA), number of hydrogen bond donors (nHD), number of rotatable bonds (nrot), number of rigid bonds (nrig), molecular flexibility (fx), molar refractivity (MR, in m^3/mol), and topological polar surface area (TPSA, in $Å^2$). The number of rotatable and rigid bonds were derived from Admetlab3.0, and used to calculate the molecular flexibility (fx), defined by:

$$fx = nrot / nrig$$

Table 2:
Physico-chemical Parameters of Investigated Compounds

No.	Formula	MW	Log P	nHA	nHD	nrot	nrig	fx	MR	TPSA
1A	C15H10O6	286.24	1.70	6	4	1	18	0.06	76.01	111.13
2A	C15H14O6	290.27	1.47	6	5	1	17	0.06	74.33	110.38
3A	C16H18O9	354.31	0.96	9	6	5	15	0.33	83.50	164.75
4A	C8H8O4	168.15	1.40	4	2	2	7	0.29	41.92	66.76
1P	C8H7NS	149.21	2.19	1	0	2	8	0.25	45.38	44.45
2P	C14H19NO9S2	409.43	0.95	10	5	7	15	0.47	91.57	199.79
3P	C8H10N2S	166.24	1.67	0	2	3	7	0.43	49.52	70.14
4P	C7H6O3	138.12	0.85	3	2	1	7	0.14	35.42	57.53

Given the established nutritional and therapeutic properties of avocado and papaya, physico-chemical analysis was first used to assess the potential oral therapeutic efficacy of the eight studied compounds.

The molecular weights (MW) of the avocado-derived compounds ranged from 168 to 354 g/mol, all within the acceptable range under Lipinski's rule. Regarding lipophilicity (Log P), which reflects a molecule's interaction with lipophilic environments and, consequently, its ability to be absorbed and distributed within the body, compounds 1A (1.70) and 1P (2.19) are likely to penetrate the skin more effectively. Summed Log P values for avocado (1A–4A) and papaya (1P–4P) compounds were 5.53 and 5.66, respectively, suggesting similar and favourable bioavailability across all compounds.

The number of hydrogen bond acceptors (nHA) varied from 4 to 9 for avocado compounds and from 0 to 10 for papaya compounds—both ranges aligning with Lipinski's criteria. However, compound 3A from avocado slightly exceeded the hydrogen bond donor (nHD) threshold, with a value of 6, while all papaya compounds conformed to the limit.

Hydrogen bonding significantly contributes to the stability of molecular complexes (Kasende et al., 2017). Avocado compounds demonstrated higher overall potential for hydrogen bonding interactions, with a combined total of 25 acceptor sites and 17 donor sites, compared to 14 acceptor sites and 9 donor sites for papaya compounds—indicating possibly greater interaction with biological targets.

Molecular flexibility is crucial for effective biological activity. Papaya compounds demonstrated generally higher flexibility values (fx), suggesting potentially enhanced binding interactions and systemic activity. Molecular refractivity (MR), which correlates with density, polarity, and van der Waals interactions, remained within the optimal range (40–130 m^3/mol) for all compounds, except 4P (papaya), which had a slightly lower MR of 35.42 m^3/mol.

Lastly, the topological polar surface area (TPSA) provides insight into a molecule's polarity and its ability to permeate cell membranes. Ideally, TPSA should lie between 20 and 140 Å² for optimal absorption. Most compounds fell within this range, with two exceptions: compound 3A (avocado) and 2P (papaya), which exhibited elevated TPSA values of 164.75 Å² and 199.79 Å², respectively—suggesting reduced absorption efficiency.

Bioavailability Radar

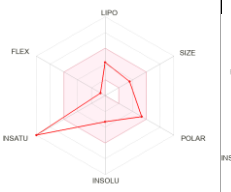
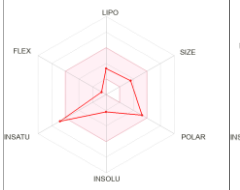
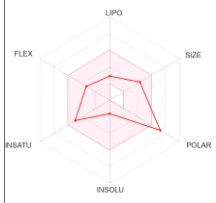
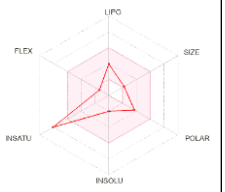
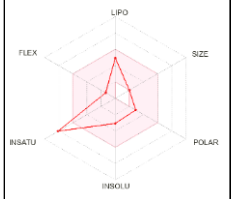
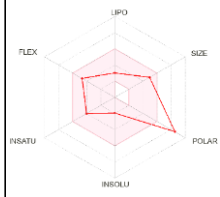
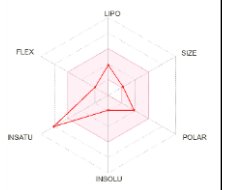
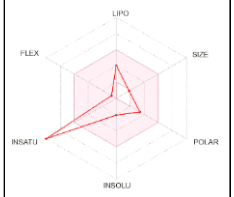
The assessment of physicochemical properties using ADMET prediction tools often produces results in the form of radar plots or "radar diagrams". These graphical representations allow for the simultaneous visualisation of multiple variables, enabling the comparison of characteristics across different samples or compounds.

A radar diagram comprises an axis for each measured variable. The values of each variable are plotted along their respective axes and connected to form a polygon. The extent of the area covered by this polygon reflects the magnitude of the properties—larger areas indicating more pronounced characteristics.

In this study, the radar diagrams incorporate six key parameters: lipophilicity (LIPO), flexibility (FLEX), polarity (POLAR), unsaturation (INSATU), size (SIZE), and insolubility (INSOLU). For each of the eight studied compounds, these diagrams are presented in **Table 3**. The pink area on each radar represents the optimal physicochemical range associated with favourable bioavailability. Ideally, a drug-like compound's radar plot should lie entirely within this pink zone.

The bioavailability radar charts show that none of the eight compounds fall completely within the optimum range. Notably, six compounds exhibit non-ideal unsaturation (1A, 2A, 4A, 1P, 3P, and 4P), while two compounds lack optimal polarity (3A and 2P). Among the avocado-derived compounds, compound 2A demonstrates the best predicted bioavailability, followed by compound 3A. For papaya, compounds 1P and 3P show the most favourable profiles. Interestingly, compounds 1A (avocado) and 4P (papaya) display similar radar profiles, suggesting comparable bioavailability characteristics.

Table 3:
Bioavailability radar diagrams of the studied compounds

1A 	**2A** 	**3A** 
4A 	**1P** 	**2P** 
3P 	**4P** 	**LEGEND** **LIPO = LIPOPHILICITY** **SIZE = MOLECULAR WEIGHT** **POLAR = POLARITY** **INSOLU = INSOLUBILITY** **INSATU = UNSATURATION** **FLEX = FLEXIBILITY**

Toxicological Assessment

Various toxicity evaluation criteria were estimated using specialised in silico tools to assess the safety profiles of the investigated compounds. For molecules intended for cosmetic applications—especially those applied to the skin—particular toxicological parameters must be considered due to their potential for systemic absorption.

The evaluated parameters included skin permeability (log Kp), blood-brain barrier permeability (log BB), skin sensitisation (SS), carcinogenicity (Cgty), mutagenicity (Ames test), eye irritation (EI), and eye corrosion (EC). The outcomes for all these parameters are summarised in **Table 4**. These results were generated using the pkCSM and ADMETlab 3.0 software packages. Notably, data for log Kp, log BB, and skin sensitisation were derived from pkCSM, while results for eye irritation and corrosion were obtained exclusively from ADMETlab 3.0.

The skin serves as a critical barrier that prevents transepidermal water loss and the entry of potentially harmful substances. Skin permeability is described by the permeability coefficient (Kp), representing the extent to which a compound can penetrate the skin via passive diffusion, governed by Fick's Law:

$$J = Kp \times C$$

where J is the flux of the compound per unit area and time, and C is the concentration at the skin surface.
The logarithm of Kp (log Kp) is thus an important index of a molecule's dermal absorption potential. For sunscreen products, a recommended threshold for acceptable skin penetration is log Kp > -2.5 cm/h.

All eight investigated compounds demonstrated acceptable skin penetration profiles, making them suitable candidates for inclusion in sunscreen formulations aimed at protecting the skin against ultraviolet (UV) radiation. Interestingly, all four avocado-derived compounds exhibited identical log Kp values (2.735 cm/h), indicating uniform dermal absorption potential.

In contrast, compounds 1P, 3P, and 4P, derived from papaya, displayed slightly lower values, falling below the 2.5 cm/h threshold. While still within a broadly acceptable range, this suggests a relatively lower passive skin permeability for these molecules.

It is important to highlight that the inclusion of permeation enhancers or formulation excipients could significantly improve dermal absorption. Such strategies may be adopted to optimise the cutaneous bioavailability of both papaya- and avocado-based sunscreen formulations.

Toxicological Parameters of the Investigated Compounds

Table 4 presents the toxicological profiles of the studied compounds, including their skin permeability (log Kp), blood-brain barrier permeability (log BB), skin sensitisation (SS), carcinogenicity (Cgty), mutagenicity (Ames test), and potential for eye irritation (EI) and corrosion (EC).

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Table 4:
Toxicological parameters of the investigated compounds

Compound	Log Kp (cm/h)	Log BB	SS	Cgty	Ames Test	EI	EC
1A	2.735	-1.23	Negative	Negative	Negative	Negative	Negative
2A	2.735	-1.07	Negative	Negative	Positive	Negative	Negative
3A	2.735	-1.42	Negative	Negative	Negative	Negative	Negative
4A	2.735	-0.42	Negative	Negative	Negative	Positive	Negative
1P	1.248	0.46	Positive	Negative	Negative	Negative	Negative
2P	2.735	-1.60	Negative	Negative	Negative	Negative	Positive
3P	2.332	-0.14	Negative	Negative	Negative	Positive	Negative
4P	2.392	-0.33	Negative	Positive	Negative	Negative	Negative

Blood-Brain Barrier Permeability

The blood-brain barrier (BBB) is a selective and protective interface of the central nervous system (CNS), preventing harmful substances—including toxins, pathogens, and carcinogens—from entering the brain. Molecules designed for peripheral action, such as in topical formulations, are not expected to cross the BBB. A low BBB permeability is therefore preferable in the context of dermally applied cosmetic products.

The parameter log BB, defined as the logarithm of the brain-to-blood concentration ratio at equilibrium, serves as an indicator of a compound's ability to cross the BBB. According to pkCSM software predictions, all compounds exhibited log BB values below the threshold of 0.3, with the exception of compound 1P (benzyl isothiocyanate), which displayed a value of 0.46. This positive value suggests a high degree of BBB permeability, rendering it unsuitable for use in sunscreen formulations in its unmodified form.

Carcinogenicity and Mutagenicity

Among the eight compounds assessed, most were non-carcinogenic and non-mutagenic, with two exceptions:

1. Compound 2A was identified as mutagenic (positive Ames test).
2. Compound 4P showed potential carcinogenicity.

These findings indicate that, while generally safe, select compounds may pose specific genotoxic risks and require further investigation or exclusion depending on formulation context.

Skin Sensitisation

Skin sensitisation, also referred to as Type IV hypersensitivity, represents a medium-term immunological reaction caused by recurrent exposure to sensitising agents. It is of significant concern in cosmetic formulation due to the potential for allergic contact dermatitis.

Only compound 1P was predicted to be a skin sensitiser, raising safety concerns for its inclusion in products designed for regular topical application.

Eye Irritation and Corrosion

Evaluating the potential for eye irritation and corrosion is essential in product development, particularly for dermal formulations that may inadvertently contact the eye region.

1. Eye irritation (EI), characterised by transient symptoms such as redness and itching, was predicted for compounds 4A and 3P.
2. Eye corrosion (EC), a more serious and often irreversible condition caused by chemical burns, was predicted for compound 2P only.

Hence, particular caution is warranted when formulating with these compounds, especially around sensitive facial regions.

Comparative Toxicological Assessment

Taken as a whole, the avocado-derived compounds (1A–4A) demonstrated a more favourable toxicological profile compared to the papaya-derived compounds (1P–4P). The latter group exhibited higher BBB permeability, skin sensitisation, carcinogenic potential, and ocular risks in select compounds.

Physico-Chemical Parameters and Toxicity: Application of Pfizer and GSK Rules

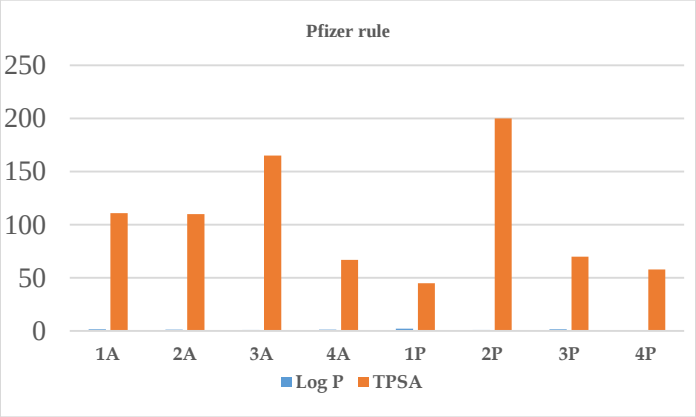
To further interpret the toxicological relevance of the compounds' physico-chemical properties, the Pfizer and GSK (GlaxoSmithKline) rules were applied. These rules help predict toxicity risks based on compound characteristics such as lipophilicity, molecular weight, and polar surface area.

Pfizer Rule

Often misattributed as Lipinski's Rule, the Pfizer 3/75 rule posits that compounds with log P > 3 and TPSA < 75 Å²

are more likely to exhibit toxicity (Waring et al., 2015). As shown in **Figure 5**, none of the studied compounds simultaneously met both of these criteria. Although compounds 4A, 1P, 3P, **and** 4P had TPSA values below 75 Å², none had log P values exceeding 3. This suggests that all eight compounds are compliant with the Pfizer rule, supporting a favourable toxicological profile.

Figure 5:
Pfizer rule: Relationship between log P and TPSA

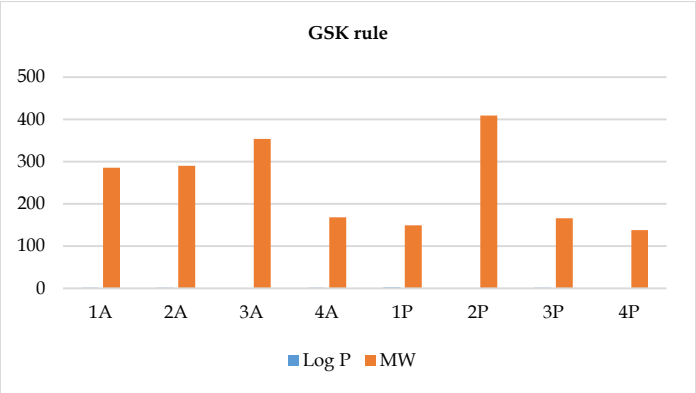


GSK Rule

Based on an extensive analysis by Gleeson (2008), the GSK rule indicates that compounds with a molecular weight below 400 g/mol and log P below 4 generally exhibit desirable pharmacokinetic and toxicological profiles.

All eight compounds satisfied both criteria, as illustrated in **Figure 6**, and are thus considered compliant with the GSK rule, further reinforcing their suitability for use in dermal formulations.

Figure 6:
GSK rule: Relationship between log P and molecular weight



CONCLUSION

The skin, although equipped with natural protective mechanisms, requires additional measures, such as sun protection creams, to prevent damage caused by ultraviolet rays. While commonly used, sunscreens can have adverse effects, highlighting the need for alternative solutions. This justifies the use of plant-based cosmetics. However, although these compounds are naturally occurring, they may still possess some toxicity. To reduce the need for experimental studies on animals, computational toxicology allows for the establishment of toxicological profiles based on experimental data, using structure-activity relationships.

The objective of this study was to evaluate the toxicological profiles of four avocado compounds and four papaya compounds used in sunscreen formulations due to their antioxidant properties, through a computational approach. Analysis of physico-chemical properties, pharmacokinetic parameters, and bioavailability radar showed that none of the investigated compounds fully resides in the optimal zone. However, compounds 2A, 3A, 1P, and 3P only deviate slightly from the optimal zone. A thorough analysis of the physico-chemical parameters of each compound in relation to its toxicity, using the Pfizer and GSK rules, found that all the investigated compounds exhibited fairly good toxicological profiles. The data for each analyzed toxicity descriptor indicated that compound 4P was likely to induce cancer, compound 2A was mutagenic, and compounds 4A and 3P were found to be eye irritants.

Although in silico techniques are useful for preliminary predictions, they cannot completely replace real biological tests (*in vitro* and *in vivo*), which allow hypotheses to be validated and biological effects to be observed in a complex, dynamic environment.

Ethical Approval: The study protocol received ethical approval from the Department of Chemistry, Faculty of Science and Technology, University of Kinshasa, Kinshasa, Democratic Republic of the Congo.

Conflicts of Interest: None declared.

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