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Communication

Promising Safety Profile of Hesperidin: A Comprehensive Toxicity Assessment among Investigated Flavonoids

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Abstract: This study focuses on the toxicity assessment of various flavonoids, with particular emphasis on Hesperidin. Among the investigated compounds, Hesperidin exhibits notable potential and low toxicity in both short and long-term evaluations. The toxicity parameters for Hesperidin include a low Max. Tolerated Dose (Human) (0.525 log mg/kg/day), indicative of its minimal potential harm to humans. Additionally, its Oral Rat Acute Toxicity (LD50) (2.506 mol/kg) suggests a relatively low acute toxicity level. The Oral Rat Chronic Toxicity (LOAEL) (3.167 log mg/kg_bw/day) signifies a higher dose threshold for observing adverse effects over the long term. Furthermore, Hesperidin demonstrates low Minnow Toxicity (7.131 log mM), suggesting minimal impact on aquatic organisms. Overall, this comprehensive assessment positions Hesperidin as a promising flavonoid with favorable properties and minimal toxicity.

Keywords: Hesperidin; flavonoids; polyphenols,pkCSM tool

1. Introduction

Polyphenols, are a diverse group of natural compounds found in plants. Their antioxidant properties make them valuable in combating the damage caused by free radicals, which are associated with aging and various diseases [1,2].

The subclasses of polyphenols, such as flavonoids, phenolic acids, and polyphenolic amides, each contribute different compounds with unique properties. These substances are present in a variety of foods, including fruits, vegetables, tea, coffee, red wine, and certain whole grains [3,4].

Consuming a diet rich in polyphenol-containing foods has been associated with potential health benefits, such as anti-inflammatory, anticancer, antiviral, and neuroprotective effects. However, as with any nutritional component, the specific health effects can depend on factors such as the type and amount of polyphenols consumed, as well as individual variations [1–4]. In a short communication, the focus is on predicting the toxicity properties of flavonoids using the pkCSM Database [5].

Flavonoids, also known as bioflavonoids, are polyphenolic secondary metabolites found in plants, commonly consumed in human diets due to their presence in fruits, vegetables, and other plant-based foods. The term "flavonoid" is derived from the Latin word "flavus," meaning yellow, reflecting their natural color [6–8].

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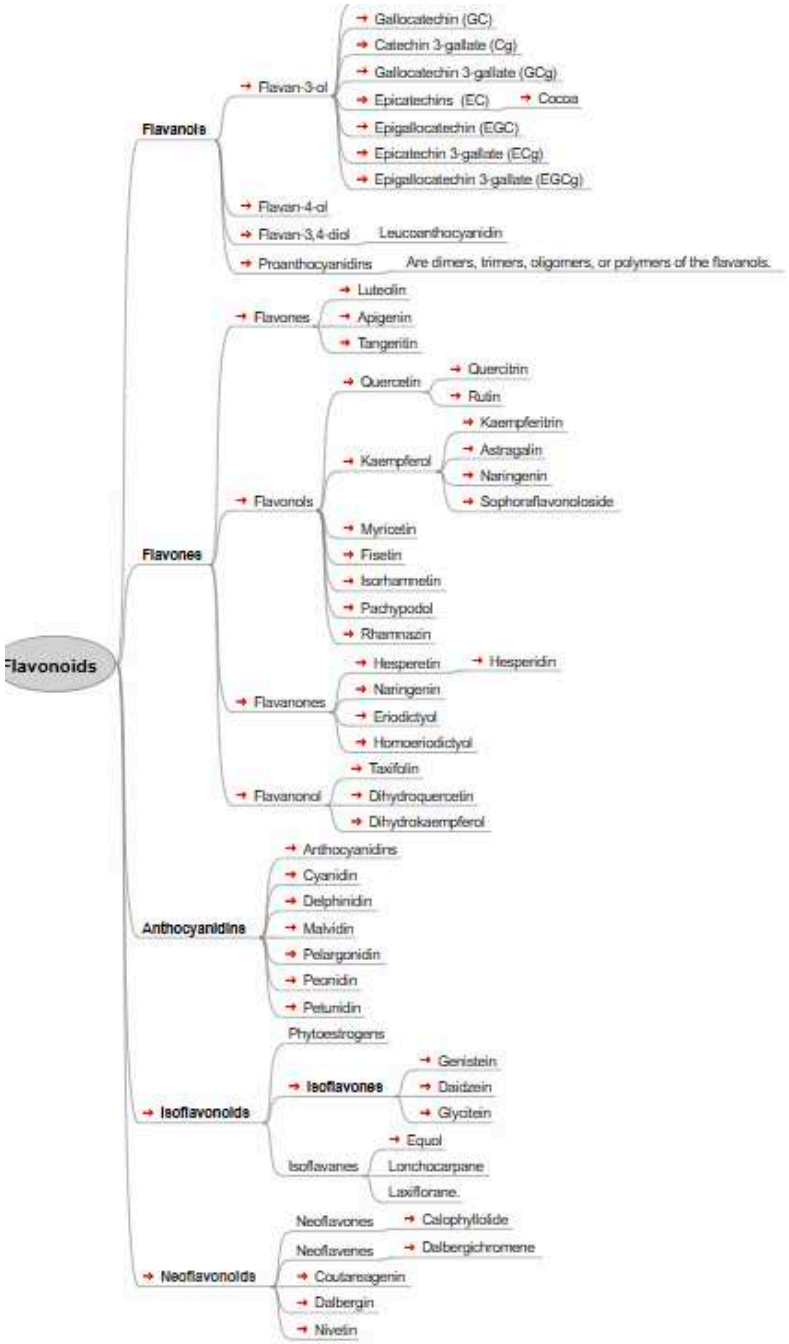

Figure 1. displays the chemical structures of the main flavonoids studied in a particular investigation.

2. Material and Methods

The research conducted by Pires, Blundell, and Ascher involves the development and application of the pkCSM tool [5], designed for predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. In a specific application, the study investigates the toxicity properties of various flavonoids.

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3. Results and Discussion

This communication offers a broad perspective on polyphenols, highlighting their diverse presence in plants and underscoring their antioxidant properties with associated health benefits. The main focus of the communication is the introduction of a short study centered on predicting the toxicity properties of flavonoids. This prediction is carried out using the pkCSM Database [5], a tool designed for such computational analyses. The outcomes of this investigation are presented in Table 1, providing a tabular representation of the results obtained. From these results collectively suggest that Hesperidin exhibits promising properties with a low indication of toxicity across various measures, making it a potentially favorable compound.

In the assessment of various flavonoids, Hesperidin emerges as a standout with exceptional potential and a notable lack of toxicity in both short and long-term evaluations. The specific toxicity parameters for Hesperidin are as follows:

Max. Tolerated Dose (Human) (log mg/kg/day): Hesperidin exhibits a low potential for toxicity, as indicated by the relatively low value of 0.525 log mg/kg/day for the maximum tolerated dose in humans.

Oral Rat Acute Toxicity (LD50) (mol/kg): The LD50 value of 2.506 mol/kg suggests a relatively low acute toxicity in oral exposure, with a higher dose needed to cause harm to 50% of test subjects.

Oral Rat Chronic Toxicity (LOAEL) (log mg/kg_bw/day): Hesperidin shows a favorable chronic toxicity profile with a LOAEL value of 3.167 log mg/kg_bw/day, signifying a higher dose before observing adverse effects.

Minnow Toxicity (log mM): In terms of minnow toxicity, Hesperidin demonstrates a low level of toxicity with a value of 7.131 log mM, suggesting a minimal impact on these aquatic organisms

In conclusion, the toxicity assessment of various flavonoids, with a specific focus on Hesperidin, reveals promising findings regarding its safety profile.

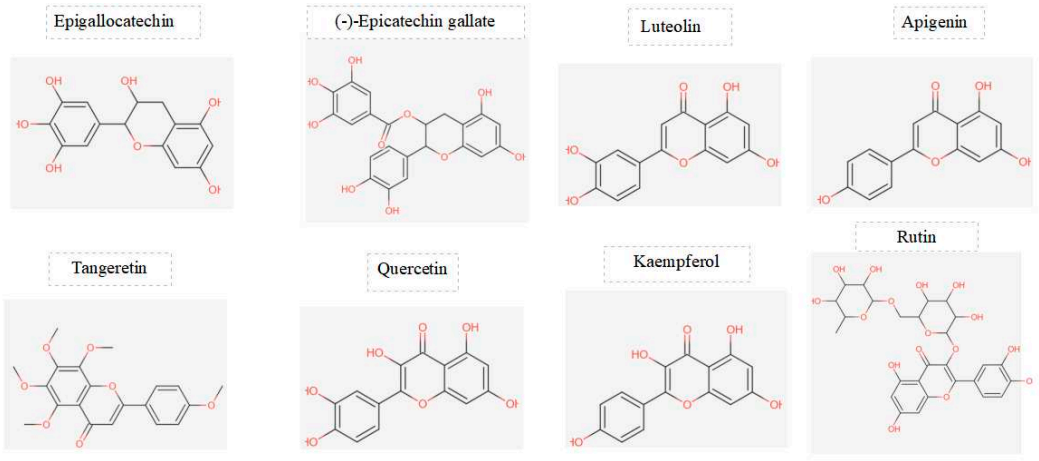

Figure 2. displays the chemical structures of the main flavonoids studied in a particular investigation.

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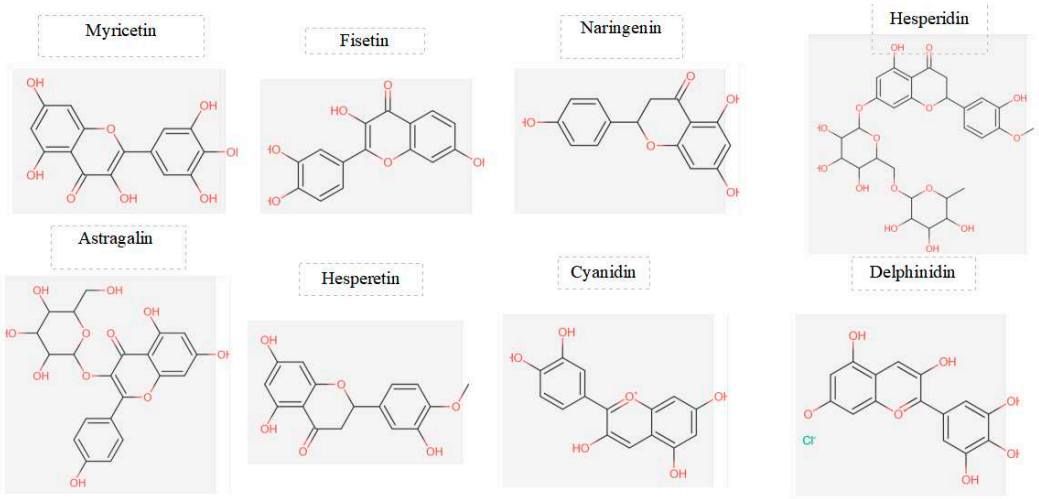

Figure 3. displays the chemical structures of the main flavonoids studied in a particular investigation.

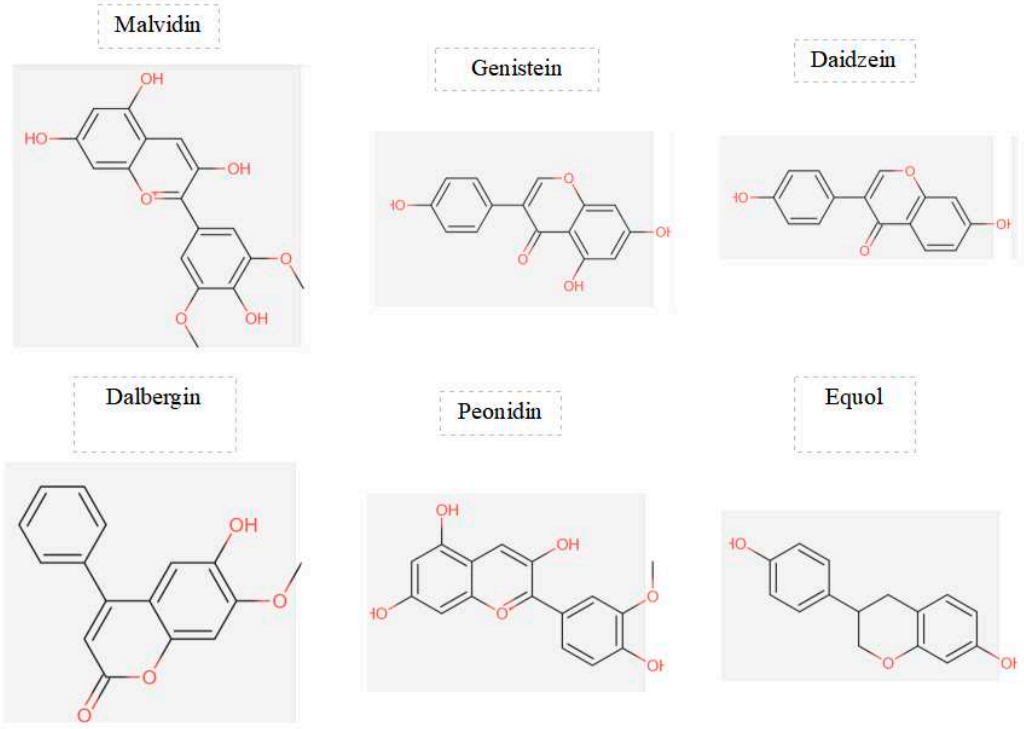

Figure 4. displays the chemical structures of the main flavonoids studied in a particular investigation.

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Table 1. the comparison of predicted toxicity properties of flavonoids using the pkCSM Database.

Compounds	AMES toxicity	Max. tolerated dose (human) (log mg/kg/day)	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)
Epigallocatechin	No	0.506	2.492	2.927	no	no	0.286	4.235
Luteolin	No	0.499	2.455	2.409	no	no	0.326	3.169
(-)-Epicatechin gallate	No	0.449	2.558	2.777	no	no	0.285	6.146
Apigenin	No	0.328	2.45	2.298	no	no	0.38	2.432
Tangeritin	No	0.385	2.368	0.944	no	no	0.355	0.144
Quercetin	No	0.499	2.471	2.612	no	no	0.288	3.721
Kaempferol	No	0.531	2.449	2.505	no	no	0.312	2.885
Rutin	No	0.452	2.491	3.673	no	no	0.285	7.677
Myricetin	No	0.51	2.497	2.718	no	no	0.286	5.023
Fisetin	No	0.579	2.465	1.921	No	No	0.376	2.273
Astragalin	No	0.582	2.546	4.53	No	No	0.285	6.735
Naringenin	No	-0.176	1.791	1.944	No	No	0.369	2.136
Hesperidin	**No**	**0.525**	**2.506**	**3.167**	**No**	**No**	**0.285**	**7.131**
Hesperetin	No	0.25	2.042	2.605	No	No	0.39	2.305
Cyanidin	No	0.497	2.464	2.542	No	No	0.29	2.548
Delphinidin	No	0.503	2.548	3.09	No	No	0.286	3.85
Malvidin	No	0.554	2.346	2.412	No	No	0.327	1.224
Genistein	No	0.478	2.268	2.189	No	No	0.377	No
Daidzein	No	0.187	2.164	1.187	No	No	0.693	1.035
Dalbergin	No	0.097	2.012	0.889	No	No	0.467	0.581
Peonidin	No	0.568	2.408	2.434	No	No	0.319	1.409
Equol	No	-0.497	2.384	1.924	No	No	0.849	1.76

4. Conclusions

Among the compounds studied, hesperidin stands out, showing excellent potential properties and demonstrating low toxicity in both short- and long-term evaluations. Parameters, including Max. Tolerated Dose (Human), Acute Oral Rat Toxicity (LD50), Chronic Oral Rat Toxicity (LOAEL), and Minnow Toxicity collectively contribute to a favorable characterization of hesperidin.The low Max. tolerated dose (human) suggests minimal potential for harm to humans, while the acute oral rat toxicity (LD50) indicates a relatively low level of acute toxicity. The chronic oral toxicity value for rats (LOAEL) suggests a higher dose threshold for observing adverse effects over a prolonged period. Furthermore, the low toxicity of minnows highlights the minimal impact of hesperidin on aquatic organisms.

These findings collectively position hesperidin as a promising candidate among flavonoids, demonstrating not only its potential health benefits but also its safety with minimal adverse effects. Further research and exploration of the therapeutic potential of hesperidin, taking into account its favorable toxicity profile, could contribute to its use in various applications, including pharmaceutical and nutritional contexts.

Authors Contributions: Protocol designed by IVF . All authors read and approved the final manuscript.

Conflict of Interest: Authors declare that they do not have any conflict of interest

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