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Possible toxicological properties of catechin from processed rose wastewater

Yana Koleva[1*], *Viktoria* Trifonova[1], *Milena* Miteva[2], *Elisaveta* Todorova-Koynova[3] and *Ana* Dobreva[4]

[1] Department of Chemistry, Faculty of Natural Sciences, University "Prof. Dr. Assen Zlatarov" Burgas, Bulgaria
[2] Faculty of Technical Sciences, University "Prof. Dr. Assen Zlatarov" Burgas, Bulgaria
[3] University "Prof. Dr. Assen Zlatarov" Burgas, Bulgaria
[4] Department of Aromatic and Medicinal Plants, Institute for Roses and Aromatic Plants, Agricultural Academy, Kazanlak, Bulgaria

Abstract. The positive effect of catechins has been proven with their antimicrobial, antiviral, anti-inflammatory and antioxidant actions for organisms, i.e. have important biological significance. More pharmacological functions have been discovered with catechins in-depth research. Catechins have various uses, such as controlling obesity, scavenging free radicals, delaying aging, inhibiting human pathogenic bacteria without harming the reproduction of beneficial bacteria, etc. The task of the work is to determine the properties (toxic) and environmental fate of catechin by means of *in silico* metods.

1 Introduction

Catechin and the structurally similar epicatechin and epigallocatechin gallate are flavonoids part of the polyphenolic group of flavanols found in plants and fruits [1]. Different tannins compounds are generated by the molecular condensation of these compounds. Catechins have the ability to suppress oxidative stress in the body, help prevent and treat cognitive and degenerative disorders [2], cardiovascular disorders [3] and exhibit pronounced bactericidal activity [4-6]. The flavonoids, and in particular catechins, is with registered availability in wastewater from the processing of industrially grown in Bulgaria varieties of rose crops [7, 8]. The presence of these and other secondary plant metabolites in wastewater poses an environmental risk. The reason is that such components even of natural origin change not only the organoleptic characteristics of wastewater, but are also capable of exhibiting toxicity. This is taken into account by environmental legislation, because falling untreated in ponds or in the soil have adverse effects on the vital activity of various organisms and plants, worsening the quality of soil and water, including groundwater [9].

Different techniques are applied to restore the quality of polluted water [10,11]. A modern approach is the use of the capabilities of membrane technology, which has proven its techno-economic efficiency, applied alone or combined and hybrid.

* Corresponding author: ykoleva@btu.bg

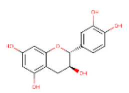
The task of the work is to determine the properties (toxic) and environmental fate of catechin by means of *in silico* metods.

2 Materials and methods

2.1 Compound data

Catechin is presented in Table 1 [12]. The separation of flavonoids and in particular flavanol (Catechin) can be achieved by a baromembrane process using a polyacrylonitrile membrane. Name and chemical structure of the compound is presented in Table 1.

Table 1. Name and chemical structure of the compound (Catechin).

Chemical name	Chemical structure
Catechin	

2.2 CompTox Chemistry Dashboard

The free and accessible web-based application Dashboard was used, which has access to nine databases of chemical compounds [13, 14].

2.2.1 Environmental fate and transport

Models (EPI Suite models, NICEATM, TEST and OPERA) and online databases have been applied to predict properties such as the adsorption coefficient, atmospheric hydroxylation rate, biodegradation half-life, fish biotransformation half-life, as well as parameters to assess bioaccumulation potential (bioaccumulation factors and bioconcentration factors) [15, 16].

2.2.2 Chemical properties

Experimental and predicted physical and chemical properties, such as logP (log octanol-water partition coefficient), S (water solubility), MP (melting point) and others, were used. Experimental and predicted data are presented in two separate tables [8, 9].

The polyacrylonitrile (PAN) membrane was obtained by the phase inversion method from a 16 wt. % solution of PAN (produced by LUKOIL Neftochim Bourgas Co., Bulgaria) in N,N - dimethylformamide (DMF) purchased from Fluka (Switzerland) [10]. The membrane has an asymmetric structure with molecular weight cut-off of 25 kDa. Membrane treated water is a waste product from the technological treatment of fresh flower from an industrially grown oil-bearing rose. oil rose. The baromembrane process for wastewater was carried out on a laboratory filtration cell SM-165-26 ("Sartorius", England).

The determined values of total flavonoids expressed as quercetin equivalents, by adding 10% Al $(NO_3)_3.9H_2O$, 1 M $C_2H_3KO_2$ and H_2O to the sample according to methodology [11]. The concentration of flavonoids is calculated by the equation of the constructed standard curve y=2.8575.x+0.21476, R^2 = 0.9737 at λ=410 nm.

3 Results and discussion

Waste water from the hydrodistillation of flower of a flower of a variety Rosa damascena Mill are subjected to membrane filtration in laboratory conditions. The waters were found to contain 7.8 mgQeE/ml of total flavonoids. The content of total flavonoids in the permeate (filtrate) was determined under different conditions according to the applied pressure, and the reduction of the filtered sample with an initial volume of 300 ml was 50%.

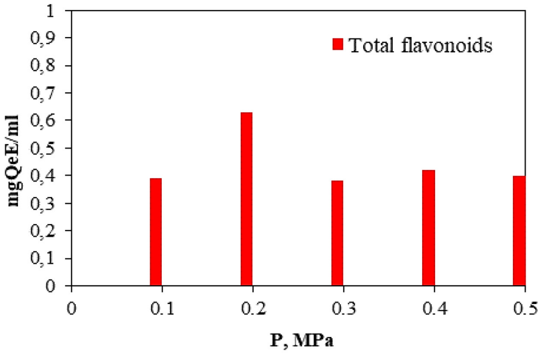


Fig. 1. Content of total flavonoids in the permeate

The concentration according to the pressure is variable, which is due to the morphology of the membrane and the specificity of the process. The lowest content in the filtrate waters is achieved at 0.3 MPa, where the concentration is only 0.38 mgQeE/ml.

The use of alternative methods to predict different properties (physicochemical and toxicological) is necessary to assess the likely hazard of a compound. Obtaining these data can be relatively quick and inexpensive and can be done in the early stages of a compound's evaluation [17].

Various properties (physical) can be evaluated, such as freezing point, boiling point, melting point, infrared spectrum, electronic parameters, viscosity, and density. Part of these physical properties are directly associated with environmental fate and health effects (e.g., electronic parameters, molecular weight, boiling/freezing point). Various software packages and algorithms have been created to predict physicochemical properties that are in good agreement with experimentally obtained values [17].

In the work, software (CompTox Chemistry Dashboard) was used to determine the physicochemical properties as well as the environmental fate of Catechin.

Physicochemical properties of Catechin as well as properties for its behavior in the environment (environmental fate (bioconcentration factor, atmospheric hydroxylation rate, biodegradation half-life, fish biotransformation half-life (Km) and soil adsorption coefficient (Koc)) are defined and arranged in Table 2.

There are three experimental data of catechin. The physicochemical properties are estimated by OPERA.

The toxic property (endpoint) is the ultimate assessment of the danger of a given substance, which includes mortality, behavior, reproductive status or physiological and biochemical changes. The obtained data on the relative toxicity of the given compound are considered by various regulatory agencies and environmental compliance groups [18].

Toxic properties (endpoints) can be acute or chronic. Acute toxicities (endpoints) examine mortality and behavior over a short period of about a week. A quantitative assessment of acute toxicity is the LD_{50}, which is considered the dose of the compound required to kill half of the organisms in the study. Chronic toxicity affects reproduction, longterm survival and growth at extremely low concentrations of the test compounds, which is for a longer period of time [18].

Table 2. Experimental and predicted properties for Catechin.

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range
Bioconcentration factor, L/kg	-	4.86	-	4.86	-	4.83-4.90
Atmospheric hydroxylation rate, ml/molecule.s	-	1.62 e-10	-	1.62 e-10	-	1.62 e-10
Biodegradation half-life, days	-	72.4	-	72.4	-	72.4
Fish biotrans-formation half-life (Km), days	-	0.309	-	0.309	-	0.309
Soil adsorption coefficient (Koc), L/kg	107	107	107	107	107	107
Polarizability, Å3	-	29.2	-	29.2	-	29.2
Henry's law, atm-m3/mole	-	2.57e-10	-	2.57e-10	-	2.57e-10
ReadyBiodeg, Binary 0/1	-	0.00	-	0.00	-	0.00
Boiling point, ºC	630	484	630	468	630	372 to 630
Flash point, °C	-	313	-	313	-	292 to 335
Melting point, °C	177	256	177	272	177	212 to 285
Molar refractivity, ml	-	73.6	-	73.6	-	73.6
Molar volume, ml	-	182	-	182	-	182
Surface tension, dyn/ml	-	88.1	-	88.1	-	88.1
Density, g/ml	-	1.63	-	1.63	-	1.59 to 1.68
logD5.5, Log10unitless	-	0.510	-	0.510	-	0.510
logD7.4, Log10unitless	-	0.510	-	0.510	-	0.510
Liquid chromatography Ret., min	-	7.99	-	7.99	-	7.99
Vapor pressure, mmHg		6.43 e-10		7.00 e-10		9.29e-17 to 1.23 e-9
Water solubility, mol/L		6.61e-2		2.23e-2		2.57e-3 to 0.217

Index of refraction,	-	1.74	-	1.74	-	1.74
LogKoa: Octanol-Air	-	9.47	-	9.47	-	9.47
LogKow: Octanol-Water	0.510	0.689	0.510	0.542	0.510	0.491 to 1.18

There is an experimental value (toxicological endpoint) for Catechin – Estrogen Receptor Binding. Results of predicted toxic properties (toxicological endpoints) for catechin were obtained by applying a Consensus method that is summed from the individual methods (Hierarchical clustering, Single model, Group contribution, Nearest neighbor).

The results of toxicological predictions (toxicological endpoints) for Catechin were obtained by software (the CompTox Chemistry Dashboard) and arranged in Table 3.

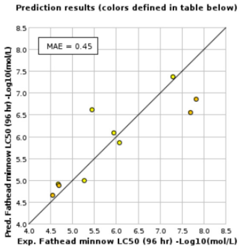
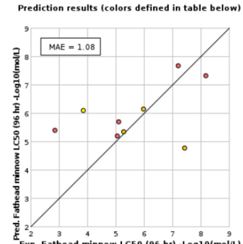
Table 3. Results of toxicological predictions (toxicological endpoints) for Catechin.

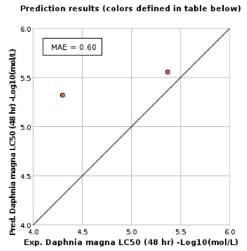
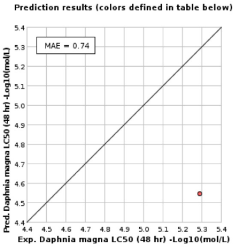
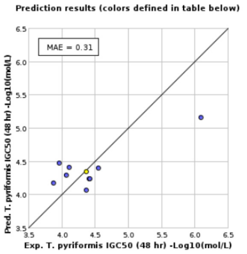
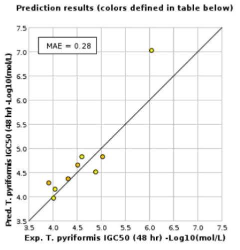
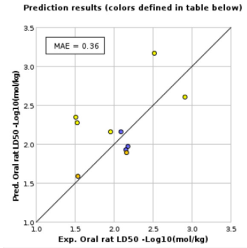
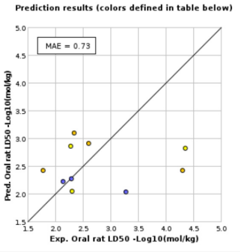
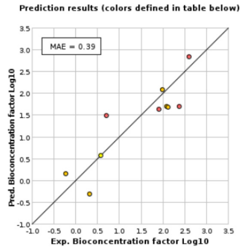
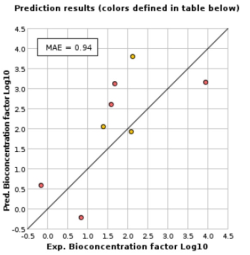
Properties	EV	C	H	SM	GC	NN
96 h Fathead minnow LC_{50}, mg/L	-	1.492	0.428	4.186	3.509	0.789
48 h *Daphnia magna* LC_{50}, mg/L	-	3.770	31.032	5.306	0.328	3.743
48 h *Tetrahy mena pyriformis* IGC_{50}, mg/L	-	10.345	30.821	-	5.443	6.599
Oral rat LD_{50}, mk/kg	-	893.689	380.956	-	-	2096.519
Bioconcentration factor	-	4.834	31.926	10.498	0.250	6.512
Developmental toxicity	-	true	true	false	-	-
Ames mutagenicity	-	true	true	-	-	false
Estrogen Receptor RBA	-	0.073	0.134	0.109	0.502	0.004
Estrogen Receptor Binding	false	true	true	true	true	false

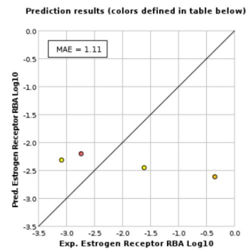
*EV – Experimental value, C – Consensus, H- Hierarchical clustering, SM –Single model, GC – Group contribution, NN- Nearest neighbor.

For each a property (toxicological endpoint), a training and an external test set are selected. Predictions were made based on similar compounds to the predicted Catechin (Table 4).

Table 4. Predicted toxicological properties of catechin from consensus method.

Toxico logical proper - ties	*Predictions for the compound (catechin) based on similar compounds in the training set*	**MAE***	*Predictions for the compound (catechin) based on similar compounds in the external test set*	**MAE***
96 h fathead minnow LC_{50}, mg/L		Entire set-0.48 Similarity coefficient ≥ 0.5 (0.45)		Entire set-0.55 Similarity coefficient ≥ 0.5 (1.08)

48 h *Daphnia magna* LC_{50}, mg/L		Entire set-0.50 Similarity coefficient ≥ 0.5 (0.60)		Entire set-0.74 Similarity coefficient ≥ 0.5 (0.74)
48 h *Tetrahymena pyriformis* IGC_{50}, mg/L		Entire set-0.28 Similarity coefficient ≥ 0.5 (0.31)		Entire set-0.33 Similarity coefficient ≥ 0.5 (0.28)
Oral rat LD_{50}, mk/kg		Entire set-0.34 Similarity coefficient ≥ 0.5 (0.36)		Entire set-0.43 Similarity coefficient ≥ 0.5 (0.73)
Bioconcentration factor		Entire set-0.42 Similarity coefficient ≥ 0.5 (0.39)		Entire set-0.51 Similarity coefficient ≥ 0.5 (0.94)
Developmental toxicity	No prediction available	Concordance-0.00 Sensitivity-N/A Specificity-0.00	No prediction available	Concordance-1.00 Sensitivity-N/A Specificity-1.00
Ames mutagenicity	No prediction available	Concordance-0.60 Sensitivity-0.60 Specificity-0.60	No prediction available	Concordance-0.90 Sensitivity-1.0 Specificity-0.67

Estrogen Receptor RBA	No prediction available			Entire set-0.76 Similarity coefficient ≥ 0.5 (1.11)
Estrogen Receptor Binding	No prediction available	Concordance-N/A Sensitivity-N/A Specificity-N/A	No prediction available	Concordance-0.86 Sensitivity-0.86 Specificity-N/A

4 Conclusions

The concentration of flavonoids in the wastewater production water was found to be 7.8 mgQeE/ml, decreasing to 0.38 mgQeE/ml after membrane filtration. Catechin has important biological effectc and studying its physicochemical and toxicological properties is essential. Research shows that experimental data on the physicochemical and toxicological properties of catechin are limited. Theoretical chemistry is important in studying the potential of a compound given limited data and information.

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