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Research Article

# Toxicological Analysis of Monoterpene Carvone: An *In Silico* Approach

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**ABSTRACT**
Many monoterpene derivatives have demonstrated activity on the SNC, including sedative, antinociceptive and antidepressant. Thus, determination of the pharmacokinetic profile (ADME) together with toxicity (ADMET) are important parameters in the definition of bioavailability and toxic effects of a molecule. The Osiris program program was used in the study for activities *in silico*. *In silico* models are being applied for the evaluation of toxicity of compound in metabolic environment of mammals. The obtained results showed the molecule of carvone was low toxicity theoretical risk.

**Keywords:** Carvone, Toxicological, *In silico*

## INTRODUCTION

The terpenoids, also known as isoprenoids, are formed by repetition branched units of five carbons, similar to units of isoprene[1].

Monoterpenes can be divided into three subgroups: acyclic (myrcene, linalool, geraniol), monocyclic (α-terpineol and terpinolene), and bicyclic (α-pinene, thujone, camphor, fenchone). In each of these subgroups, there are other classifications: unsaturated hydrocarbons (limonene), alcohols (menthol), aldehydes and ketones (myrtenal, carvone), lactones (monoterpene lactones are called iridoids, ex. nepetalactone), and tropolonas (γ-thujaplicin)[2].

In folk medicine, as in therapy plants containing terpenic derivatives have been used as sedatives, tranquilizers and anticonvulsants. Compounds as linalool, limonene and citronellol have action anticonvulsant, while menthol and myrcene, analgesic activity. Many monoterpene derivatives, for example carvone, have demonstrated activity on the SNC, including sedative, antinociceptive and antidepressant[3,4,5].

Considering the few studies on the toxic effects of the monoterpene carvone, the aim of the present study was to evaluate toxicological effects of this compost, using the *in silico* approach.

## MATERIALS AND METHODS

*OSIRIS*

Toxicity risk assessment (http://www.organic-chemistry.org/prog/peo/): while drawing a structure, the toxicity risk predictor will start looking for potential toxicity risks as long as the currently drawn structure is a valid chemical entity. Toxicity risk alerts are an indication that the drawn structure may be harmful concerning the risk category specified. Risk alerts are by no means meant to be a fully reliable toxicity prediction nor should it be concluded from the absence of risk alerts that a particular substance is completely free of any toxic effect[6].

The prediction process relies on a precomputed set of structural fragments that gives rise to toxicity alerts, in case they are encountered in the structure currently being drawn. The OSIRIS toxicity predictions resulted for mutagenicity, tumorigenicity, irritability, reproductive effectiveness, cLogP value, druglikeness and drug-score of flavonoid molecule[6].

## RESULTS AND DISCUSSION

The monoterpenes are an important class of natural products with intense flavor and odor and contains many molecules that have biological activity, including antimicrobial, and applications in the pharmaceutical, cosmetic and food[7].

Knowing that not all isolated compounds are free of toxic effects, there is the need for toxicological studies allies to pharmacological studies. The Computational Toxicology can be defined as the area of toxicology, which are applied computational and mathematical models for the prediction of adverse effects, and to better understand (s) of mechanism (s) through (s) which one (s) a substance causes damage[8].

The toxicology *in silico* one of toxicology borders brings a new paradigm for assessing the toxicity of substances, in particular, those isolated from plants in which the toxicity predictions are made using computational tools based

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QSAR (Quantitative Structure- activity Relationship), REA models (Structure-activity), statistical models,

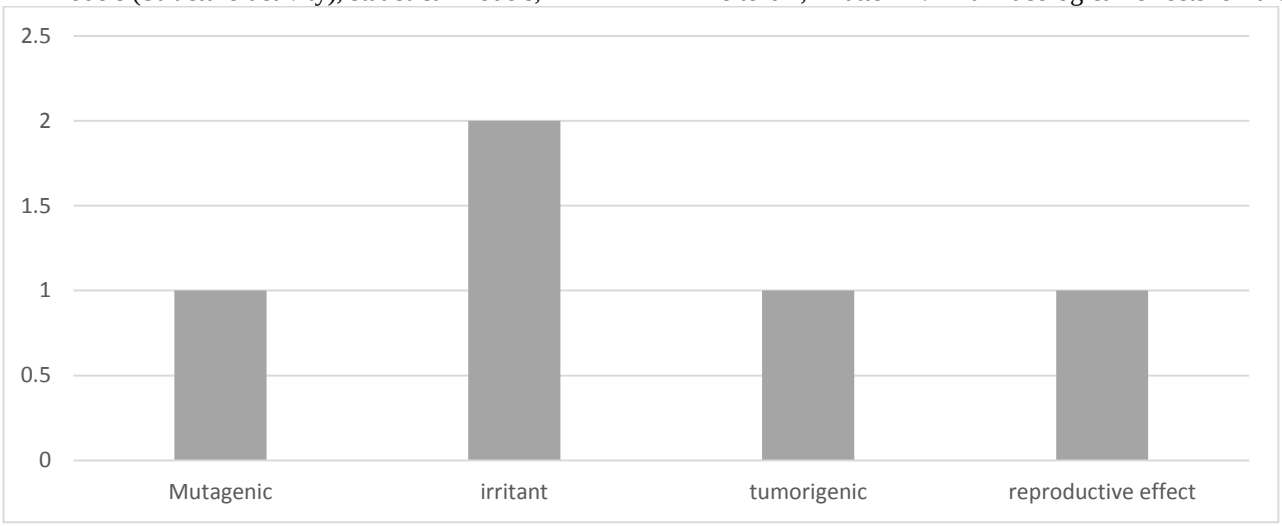


Figure 1: Risk of toxicity calculated using program Osiris Property Explorer for carvone.

among others[9]. The evaluation of the molecules *in silico* toxicity includes theoretical analysis mutagenic, tumorigenic, on the irritating and reproduction as described by Abreu (2008)[10].

The carvone was analyzed through OSIRIS tool for the determination of drug-relevant properties like mutagenic, irritant, reproductive effects, cLogP value, drug-score, druglikeness and their toxicity risks assessment. OSIRIS employed to predict the toxicity and carcinogenicity for antifungal agent was reported[11]. The results showed this monoterpene presents low theoretical risk of toxicity (Figure 1) and has considerable values druglikeness (-18,99) and drug-score (0,37). "Drug score" (combining "druglikeness", ClogP, logs, mass molecular and risk of toxicity) that generates a value infers that the potential of a compound become a future drug[12].

## CONCLUSION

*In silico* study of monoterpene carvone demonstrated that this compound has low toxicity theoretical risk.

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