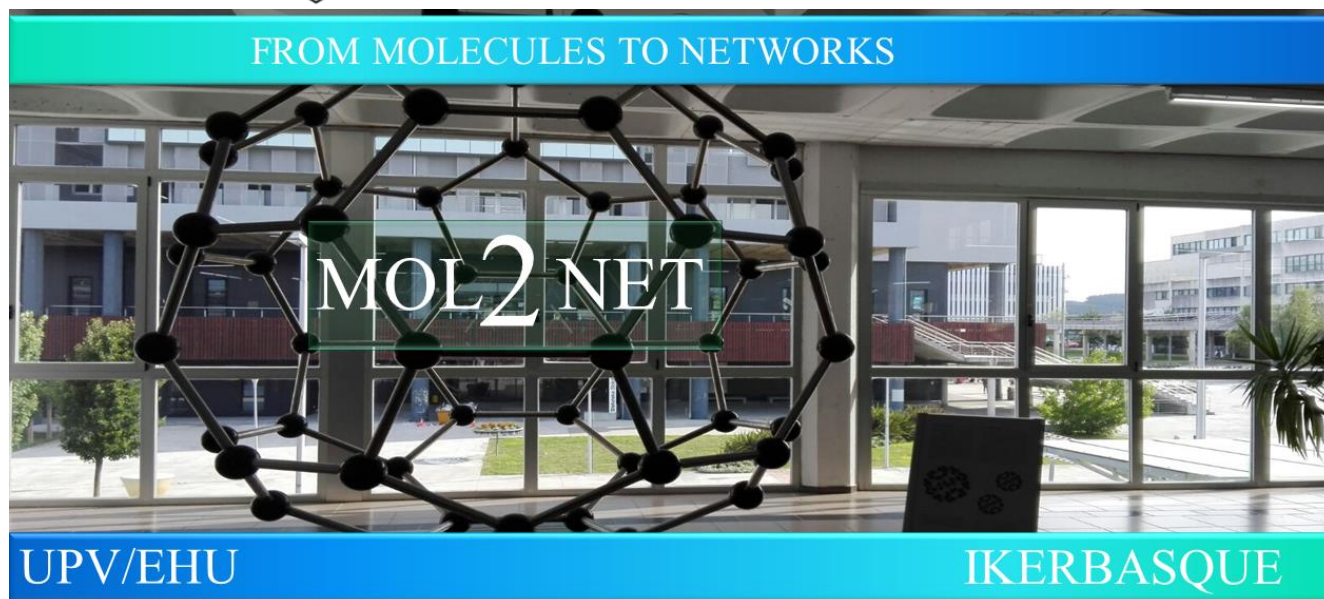




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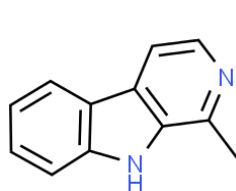
In silico comparison of anticancer properties of *Passiflora incarnata* alkaloids

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Graphical Abstract



Abstract

In this study, an *in silico* study about the anticancer properties of the *Passiflora incarnata* alkaloids was realized. As a result, these alkaloids were found to be more effective on Hs 683 Oligodendroglioma cells belonging to brain tissue with high Pa and low Pi values.

Introduction

Cancer is a disease in which some body cells proliferate out of control and invade other bodily regions [1]. It is a major public health concern in the United States and around the world, despite the amazing advancements made in its treatment. A projected 1,958,310 new instances of cancer will be diagnosed in the US alone in 2023, and 609,820 individuals will pass away from the illness. Research

on the role of several biological components like immunity, metabolism, genetics, and epigenetics in mediating these disparities is ongoing. Men are more likely than women to get bladder, colon, and brain cancer, among other cancer types [2].

It has been established that a few plant bioactive components have anti-cancer properties. An estimated 50–60% of cancer patients in the US use complementary and alternative medicine - a treatment approach that uses substances derived from various plant parts or nutrients - either exclusively or in conjunction with conventional treatment plans like chemotherapy and/or radiation therapy [3]. These include, to mention a few, lycopene from tomato, diallyl sulfide from garlic, genistein from soybean, resveratrol from grapes, sulforaphane from broccoli, isothiocyanates from cruciferous vegetables, curcumin from tumeric, genistein from soybean, apigenin from parsley, and gingerol from gingers [4].

Wild passion flower, also known as passion vine, maypop, or *Passiflora incarnata* L. (*Passifloraceae*) is a climber herb that has tasty golden berries that resemble corona-shaped blooms, brightly colored, showy flowers, and auxiliary tendrils with herbaceous or woody branches. The Latin word "Passio" which was originally discovered by Spanish explorers in 1529 and was described as a metaphor for "Christ's Passion," is the source of the expression "Passiflora." Ayurveda, Siddha, and Unani are among the traditional medical systems that have documented its therapeutic usage.

Materials and Methods

β -carboline alkaloids, including harmane, harmine, harmaline, harmol, and harmalol, are present in *P. incarnata*. In this study, the Way2Drug Platform's CLC-Pred service were used to *in silico* investigate the compounds' interactions with tumor and non-tumor cell lines as well as their potential for organ-specific carcinogenesis [5]. At the end, the higher results for each alkaloid are compared in each paragraph.

Results and Discussion

The cell line on which harmine was most effective was Hs 683 Oligodendroglioma cells belonging to brain tissue with Pa value of 0.911. In this feature, having a Pi value as small as 0.002 indicates the reliability of the result obtained within this study. It is followed by M19-MEL Melanoma cells in the skin and NCI-H295R Adrenal cortex carcinoma cells in the adrenal cortex with Pa values of 0.472 and 0.43, respectively, which are approximately 2 times lower than Hs 683 Oligodendroglioma cells.

The cell line most affected by harmaline also was Hs 683 Oligodendroglioma cells of brain tissue with Pa value of 0.841. In this feature, having a Pi value as small as 0.003 indicates the reliability of the result obtained within this study. It is followed by M19-MEL Melanoma cells in the skin and PC6 Small cell lung carcinoma cells in the lung with Pa values of 0.424 and 0.399, respectively, which are approximately 2 times lower than Hs 683 Oligodendroglioma cells.

The most affected cell line on harmol was Hs 683 Oligodendroglioma cells belonging to brain tissue with Pa value of 0.848. In this feature, having a Pi value as small as 0.003 indicates the reliability of the result obtained within this study. The next results are followed by PC-3 Prostate carcinoma in prostate and NCI-H295R Adrenal cortex carcinoma cells in adrenal cortex with 29% and 39% less (Pi 0.604 and 0.521, respectively) than other alkaloids. A-375 Malignant melanoma (Pa 0.462) and M19-MEL Melanoma cells (Pa 0.45) in the skin, DU-145 Prostate carcinoma in the prostate (Pa 0.439), RKO Colon carcinoma in the colon (Pa 0.413), HOP-18 Non-small cell lung

carcinoma cells in the lung (Pa 0.406) were affected by about 2 times less than Hs 683 Oligodendroglioma cells.

The most affected cell line by harmalol was brain tissue Hs 683 Oligodendroglioma cells with Pa value of 0.894. In this feature, having a Pi value as small as 0.002 indicates the reliability of the result obtained within this study. Then it is followed by HOP-18 Non-small cell lung carcinoma and PC6 Small cell lung carcinoma cells in the lung with Pa values of 0.468 and 0.449, approximately 2 times less than Hs 683 Oligodendroglioma cells.

And the most affected cell line by harmalol was Hs 683 Oligodendroglioma cells belonging to brain tissue with Pa value of 0.918. In this feature, having a Pi value as small as 0.002 indicates the reliability of the result obtained within this study. It is followed by M19-MEL Melanoma cells in the skin and NCI-H295R Adrenal cortex carcinoma cells in the adrenal cortex with Pa values of 0.466 and 0.446, respectively, which are approximately 2 times lower than Hs 683 Oligodendroglioma cells.

As a final result, we can note that the highest anticancer effect of all alkaloids analyzed was on Hs 683 Oligodendroglioma cells belonging to brain tissue. When comparing these alkaloids, the order of Pa values is as follows:

Harmane > Harmine > Harmalol > Harmol > Harmaline with Pa 0.918 > 0.911 > 0.894 > 0.848 > 0.841

That is, the effects of harman and harmine on Hs 683 Oligodendroglioma cells are close to each other and more than other alkaloids. Compared to other alkaloids analyzed, harmol was the alkaloid with the wide spectrum of action expressed by higher Pa values in the cell lines. In general, M19-MEL Melanoma, NCI-H295R Adrenal cortex carcinoma, PC6 Small cell lung carcinoma, HOP-18 Non-small cell lung carcinoma cells were the common points in the effect spectrum of these alkaloids. Cell lines with higher Pa values of harmol compared to other alkaloids included PC-3 Prostate carcinoma, A-375 Malignant melanoma, DU-145 Prostate carcinoma, RKO Colon carcinoma, thus indicating that harmol has both a wider and more diverse spectrum of effects.

Conclusions

Overall, these *in silico* calculations are very important in terms of both the breadth of results obtained and the cost-effectiveness. The acquainted results can be useful for obtaining new anticancer drugs by continuing with *in vitro* and clinical trials.

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