The Journal of Phytopharmacology 2021; 10(2): 80-83
Online at: www.phytopharmajournal.com

Research Article

ISSN 2320-480X
JPHYTO 2021; 10(2): 80-83
March- April
Received: 01-02-2021
Accepted: 19-02-2021

doi: 10.31254/phyto.2021.10202

V Ramakrishnan
Department of Veterinary Pharmacology and Toxicology, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

P Ravikumar
Bioinformatics Centre and ARIS Cell, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

T Raja
Bioinformatics Centre and ARIS Cell, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

K Vijayarani
Bioinformatics Centre and ARIS Cell, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

A Arivuchelvan
Department of Animal Husbandry Statistics and Computer Applications, Veterinary College and Research Institute, Namakkal – 637 002, Tamil Nadu, India

M Parthiban
Department of Animal Biotechnology, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

M Thangapandiyan
Department of Veterinary Pathology, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

SP Preetha
Department of Veterinary Pharmacology and Toxicology, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India

Correspondence:
Dr. SP Preetha
Department of Veterinary Pharmacology and Toxicology, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai – 600 007, Tamil Nadu, India
Email: drsppreetha@gmail.com

In silico evaluation of phytocompounds from Indian medicinal plants for Canine Mammary Tumours

V Ramakrishnan, P Ravikumar, T Raja, K Vijayarani, A Arivuchelvan, M Parthiban, M Thangapandiyan, SP Preetha*

ABSTRACT

Canine mammary tumours are among the most predominant neoplasms and happen all the more usually among unblemished females which are not spayed at an early age. The previous study carried out at Madras Veterinary College reported that out of the 14,326 clinical cases presented in an eight months study, 61 cases were mammary tumours. The current study was aimed to screen chemo preventive effect of phytocompounds of Indian medicinal plants for Canine mammary tumours. Mammaglobin-B was taken as a target protein and it was modeled using I-Tasser. Around 920 phytocompounds were collected from different Indian medicinal plants using Dr. Duke's database. In which, after checking Lipinski Rule of five, 132 compounds were selected for this study. The 3D structure of all the phytocompounds were retrieved from PubChem database. Docking studies were done using Discovery Studio 4.0. From the results, the phytocompounds Homocapsaicin (Libdcok score: 102.27), Homodihydrocapsaicin (Libdcok score: 101.55) and Isositsirikine (Libdcok score: 99.19) showed the best Libdcok score. Hence, the present study was concluded that the phytocompounds Homocapsaicin and Homodihydrocapsaicin from *Capsicum annuum* and Isositsirikine from *Catharanthus roseus* had potential effect against Canine mammary tumours.

Keywords: Canine mammary tumours, Mammaglobin-B, Phytocompounds, *Capsicum annuum*, *Catharanthus roseus*.

INTRODUCTION

Canine mammary tumors (CMT) are among the most predominant neoplasms and occurring unblemished females which are not spayed at an early age. Most habitually mammary organ tumors are found in bitches of 5 years or more [1]. The Madras Veterinary College, Clinics reported 14,326 clinical cases presented in eight months, out of which 157 (1.09%) cases were neoplastic, 96 (0.67%) cases had skin tumours and 61 (0.42%) cases had mammary tumours. There are different types 14326 clinical cases of mammary tumors in canines of which half them are considerate and the other half are harmful. The most widely recognized considerate types of canine mammary tumors are a blend of few unique sorts of cells. Solitary tumors have more than one sort of cell which is really uncommon in numerous species [2].

The sporting breeds of dogs including the miniature or toy Poodle, Samoyed, Great Pyrenees, Terrier Keeshond and Airedale have excess risk of developing mammary tumours whereas the mammary tumour types occurred at low risk level in mixed breeds of dog. Collies had a low incidence of benign neoplasms. Radiation treatments, chemotherapy, hostile to estrogen treatment alone have been used to treat inoperable mammary diseases [3].

The most commonly used chemotherapy protocol for the prevention of metastasis from malignant breast cancer in dogs had been adriamycin every 21 days and oral cytoxan every other day for 8 weeks or on day 3-6 of each 21 day cycle. However more recently, many oncologists have switched to the use mitoxantron (Novantrone™) as a first choice and then adriamycin or carboplatin are resistant to the disease. Treatment with chemotherapy may reduce the ability of the circulating cancer cells to metastasize to the lungs. Medical procedure incorporates modifications for every circumstance, thinking about all components viewing the neoplasm in that capacity. In this way, the accompanying circumstances are recognized: healing resection, palliative medical procedure, preventive medical procedure, analytic medical procedure, cytoreductive medical procedure [4].

Mammaglobin, it belongs to the family of secretoglobin. Overexpression of mammaglobin-B is the reason for canine mammary tumors. Quantitative real-time polymerase chain reaction (qRT-PCR) and immunohistochemistry (IHC) techniques were used to find the expression of mammaglobin-B mRNA.

Expression of this protein in the healthy mammary glands was 6.67% and 76.7% was observed as the highest level in the CMT cells [5].

Useful impact of plants commonly results from the mixes of secondary metabolites present in the plant and the significant bioactive constituents are the phenolics, flavonoids, alkaloids and tannins. Plants have been known since relic to have outstanding organic exercises including antibacterial, antioxidative and anticancer properties. Secondary metabolites are potential anticancer medications that reason either direct cytotoxicity on malignant growth cells or then again may influence procedures engaged with tumor advancement [6].

Capsicum annuum and *Euphorbia hirta* had potential cytotoxic effect against breast cancer cells and it was proved in MCF 7 cells [7, 8]. Moon *et al* (2018) [9] reported anticancer activity of *Catharanthus roseus.* Garcinol is a polyisoprenylated benzophenone found from the fruit of *Garcinia indica*. It has been reported to exhibit various pharmaceutical effects, including antimicrobial, anti-inflammatory, antioxidant, apoptotic, antitumor, anti-neurodegenerative [10]. Aqueous extract of *Terminalia arjuna* bark had potential effect against mammary tumor [11]. Methanolic extract of *Terminalia arjuna* bark had antiproliferative activity on human MCF-7 cell line by MTT assay [12]. *Thymus vulgaris L.* is an herb rich in fundamental oil and contains oxygenated monoterpenes and monoterpene hydrocarbons including thymol, carvacrol, p-cymene, borneol, trans-caryophyllene and cis-sabinene hydrate are available. Besides, *Thymus spp.* contains phenolics and flavonoid subsidiaries. These phytochemicals have noteworthy chemopreventive effects [13].

A few bioinformatics tools and databases have been utilized to create productive strategies for encouraging objective recognizable proof, as the initial phase in medication disclosure. Keeping in view the significance and favorable circumstances of mix chemotherapy utilizing ethnoveterinary prescription on the tumor cells, this examination is an endeavor to investigate the impact of herbs utilizing CADD (Computer Aided Drug Design). Bioinformatics software is not only find lead particles and to discover the connection between the structure and the action of little atoms. Thus, the present study is designed to evaluate the phytocompounds from Indian medicinal plants against canine mammary tumour using *in silico* methods.

MATERIALS AND METHODS

Ligand selection

Around 920 phytocompounds were collected from different Indian medicinal plants such as *Capsicum annuum, Catharanthus roseus, Euphorbia hirta, Terminalia arjuna* and *Thymus vulgaris* using Dr. Duke's database. After checking Lipinski Rule of five, 132 compounds were selected for the study. The 2D and 3D structure of all these compounds were retrieved from PubChem database.

Target selection

The sequence of canine target protein Mammaglobin-B was taken from UniProt database and their ID is A0A068PC33_CANLF.

Homology modelling and docking studies

As there is no 3D structure available for target protein Mammaglobin-B, the sequence was modeled using I-Tasser and it was evaluated using Ramachandran plot. Docking studies were done using Discovery Studio 4.0.

RESULTS AND DISCUSSION

Ligand and Target selection

In this study, among the 132 compounds, 10 compounds were selected as the best ligands for Canine mammary tumor. Target protein Mammaglobin-B was modeled and evaluated using I-Tasser and Ramachnadran plot, respectively and showed in Fig. 1 & 2. Modeling was done using multi template method. In the Ramachnadran plot, 86.7 % residues are present in the favored regions and it confirms that the modeled 3D structure is good.

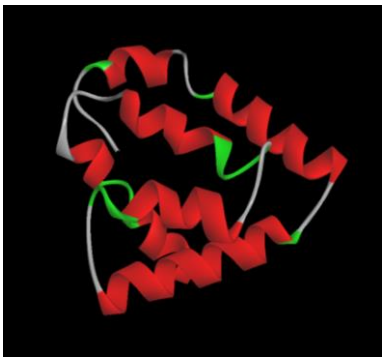

Figure 1: Modeled structure of Mammaglobin-B

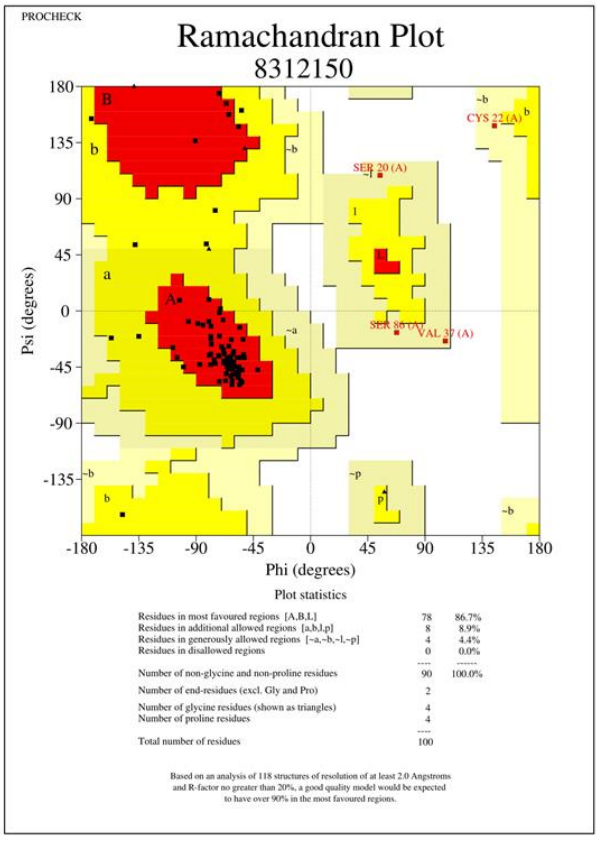

Figure 2: Ramachandran plot for the modeled structure of Mammaglobin-B

Docking studies

After checking Lipinski rule of five, 132 compounds from different Indian medicinal plants were docked with modelled 3D structure of Mammaglobin B using Discovery studio 4.0 and the results are shown in table 1. From the results, among the 132 phytocompounds, 10 compounds showed better interaction with target protein Mammaglobin B, in which, the phytocompound Homocapsaicin

showed the best Libdcok score of 102.27 with the interaction of amino acid residues MET 81 and MET 84. Homodihydro capsaicin showed better interaction with the amino acid residues of MET 81and PHE 77 and gave the Libdcok score of 101.55. The compounds Homocapsaicin and Homodihydro capsaicin are from *Capsicum annuum.* The compound isositsirikine from *Catharanthus roseus* showed good interaction with LEU 62 and gave the Libdcok score of 99.19. Besides, higher the Libdcok score indicates the better activity. However, among the ten phytocompounds lowest Libdcok score was observed in the compound Rhamnetin, Pentadecanoic acid and Serpentine. The 2D and 3D structure of docked images are shown in Fig. 3 to 8. When compared to previous report [14], the compounds like Homocapsaicin, Homodihydrocapsaicin and isositsirikinein in the current study showed very good Libdock score.

Table 1: Interaction of phytocompounds with Mammaglobin B

S. No.	PubChemCID	Compound Name	Plant Name	LibDock Score	Number of H-Bond	Interacting residues	Bond Length (Å)
1	6442566	Homocapsaicin	*Capsicum annuum*	102.269	2	MET 81	2.60
						MET 84	2.55
2	3084336	Homodihydrocapsaicin	*Capsicum annuum*	101.546	3	MET 81	2.74
						MET 81	2.91
						PHE 77	1.86
3	5377267	Isositsirikine	*Catharanthus roseus*	99.1951	1	LEU 62	2.40
4	15569773	8-hydroxyhexadecanoic acid	*Terminalia arjuna*	99.0279	2	TYR 42	1.74
						ALA 28	2.48
5	441975	Ajmalicine	*Catharanthus roseus*	98.158	1	ALA 28	2.92
6	445638	Palmitoleic acid	*Capsicum annuum*	97.112	1	LEU 46	2.45
7	5280343	Quercetin	*Euphorbia hirta*	91.7963	1	ILE 33	2.65
8	5281691	Rhamnetin	*Euphorbia hirta*	94.0286	2	THY 42	1.66
						PHE 77	2.56
9	13849	Pentadecanoic acid	*Capsicum annuum*	94.4014	1	LEU 46	2.48
10	73391	Serpentine	*Catharanthus roseus*	94.014	3	ALA 28	1.74
						LEU 62	2.92
						ILE 33	2.80

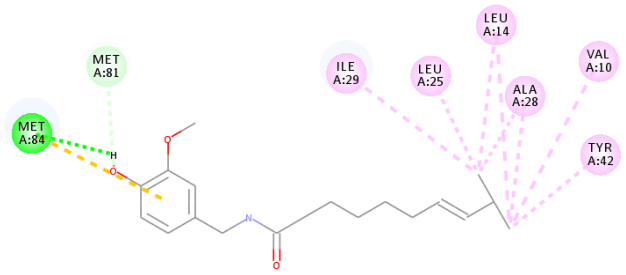

Figure 3: The 2D interaction of Homocapsaicin with Mammaglobin B

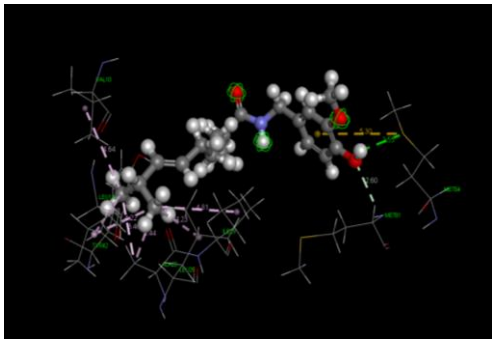

Figure 4: The 3D interaction of Homocapsaicin with Mammaglobin B

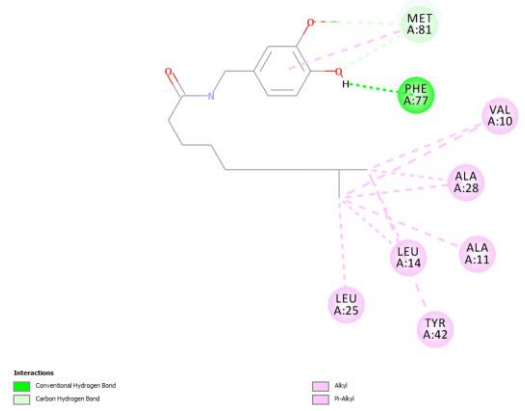

Figure 5: The 2D interaction of Homodihydrocapsaicin with Mammaglobin B

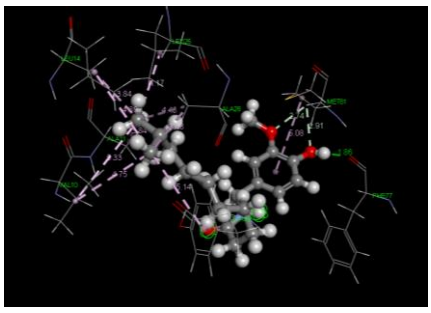

Figure 6: The 3D interaction of Homodihydrocapsaicin with Mammaglobin B

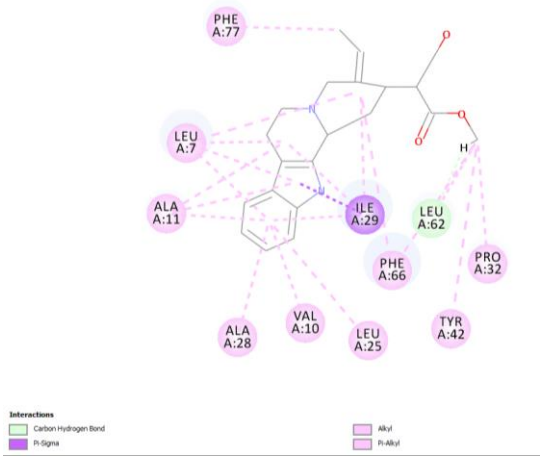

Figure 7: The 2D interaction of Isositsirikine with Mammaglobin B

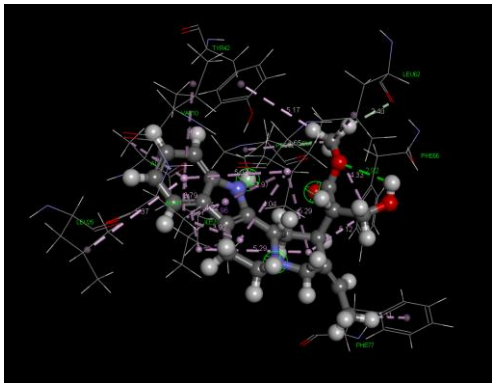

Figure 8: The 3D interaction of Isositsirikine with Mammaglobin B

CONCLUSION

Hence, the present study concludes that Homocapsaicin, Homodihydrocapsaicin from *Capsicum annuum* and isositsirikine from *Catharanthus roseus* showed very good interaction with the target protein Mammaglobin B. Further *in vitro* and *in vivo* studies are to be done to confirm chemopreventive effect of these phytocompounds which may play an essential role in the upcoming days to find the remedy for Canine mammary tumor.

Acknowledgement

The authors would like to thank DBT – BTIS Bioinformatics centre, Madras Veterinary College, Tamil Nadu Veterinary and Animal Sciences University, Chennai, Tamil Nadu, India for providing required facility to complete this work successfully under the scheme of BTISNet (No.BT/BI/13/035/2017).

Conflict of Interest

Authors declare that there is no conflict of interest.

REFERENCES

1. Murphy S. Mammary tumours in dogs and cats. In practice. 2008; 30(6):334-339.
2. Anjan Kumar KR, Rao GVS, Balachandran C. Incidence, cytology, gross pathology and histopathology of mammary tumours in dogs of Chennai. Int. J. Pharma and BioSci. 2011; 2(3):399-405.
3. Priester WA. Occurance of tumours in domestic animal-data from 12 united states and Canadian colleges. Vety. Medicine J. Natl. Cancer. Inst. 1979; 47:1333.
4. Delisle F, De Vauchelle P. Thérapeutique anticancéreuse la decision thérapeutique. Rec. Méd. Vét., Special Canc. 1990; 11(166):995–997.
5. Pandey M, Sunil Kumar BV, Gupta K, Sethi RS, Kumar A, Verma R. Over-expression of mammaglobin-B in canine mammary tumors. BMC Vet. Res. 2018; 14(1):184.
6. Bellini MF, Angeli JPE, Matuo R, Terezan AP, Ribeiro LR, Mantovani MS. Antigenotoxicity of blazei mushroom organic and aqueous extracts in chromosomal abrerration and cytokinesis block in assays in CHO-kI and HTC cells. Toxicol. in vitro. 2006; 20(3):355-360.
7. Kwan YP, Saito T, Ibrahim D, Al-Hassan FMS, Oon CE, Chen Y, Jothy SL, Kanwar JR, Sasidharan S. Evaluation of the cytotoxicity, cell-cycle arrest, and apoptotic induction by *Euphorbia hirta* in MCF-7 breast cancer cells, Pharmaceutical Biol. 2016; 54(7):1-14.
8. Yoon HJ, Lee S, Hwang IK. Effects of green pepper (*Capsicum annuum* var.) on antioxidant activity and induction of apoptosis in human breast cancer cell lines. Korean J Food Sci Tech. 2012; 44(6):750-8.
9. Moon SH, Pandurangan M, Kim DH, Venkatesh J, Patel RV, Mistry BM. A rich source of potential bioactive compounds with anticancer activities by Catharanthus roseus cambium meristematic stem cell cultures. J. Ethnopharmacol. 2018; 217:107-117.
10. Saadat N, Gupta SV. Potential Role of Garcinol as an Anticancer Agent. J. Oncol. 2012; 2012:8.
11. Liu SJ, Liu M, Li HY, Simmen RC, Johann Jr DJ. Anticancer Activity of Aqueous Extracts of Terminalia arjuna (TA) Bark. The FASEB Journal. 2019; 33(S1):816-819.
12. Shalini S, Kumar RR, Birendra S. Antiproliferative effect of Phytosome complex of Methanolic extact of Terminalia arjuna bark on Human Breast Cancer Cell Lines (MCF-7). Int J Drug Dev Res. 2015; 7(1):173-82.
13. Noroozisharaf A, Kaviani M. Effect of soil application of humic acid on nutrients uptake, essential oil and chemical compositions of garden thyme (*Thymus vulgaris L.*) under greenhouse conditions. Physiol. Mol. Biol. Plants. 2018; 24:423–431.
14. Sujatha PL, Preetha SP, Balachandran C, Kumarasamy P, Venkateswaran KV, Devaraj H. Computer-Aided Approach to Study the AntiTumour Potentials of Seaweed against Canine Breast Cancer. Int. J. Basic Appl. Biol. 2016; 3(3):206-209.

HOW TO CITE THIS ARTICLE

Ramakrishnan V, Ravikumar P, Raja T, Vijayarani K, Arivuchelvan A, Parthiban M, *et al*. *In silico* evaluation of phytocompounds from Indian medicinal plants for Canine Mammary Tumours. J Phytopharmacol 2021; 10(2):80-83.