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RESEARCH ARTICLE

Development of MLR and SVM Aided QSAR Models to Identify Common SAR of GABA Uptake Herbal Inhibitors used in the Treatment of Schizophrenia

Sahila Mohammed Marunnan[1,2], Babitha Pallikkara Pulikkal[3], Anitha Jabamalairaj[2], Srinivas Bandaru[4], Mukesh Yadav[4], Anuraj Nayarisseri[4,5] and Victor Arokia Doss[6,*]

[1]*Department of Biochemistry and Bioinformatics, Karpagam University, Coimbatore- 641 021, Tamil Nadu, India;* [2]*Department of Bioinformatics, SIAS-Centre for Scientific Research, Safi Institute of Advanced Study (SIAS), Rasiya Nagar, Vazhayoor East, Malappuram-673633, Kerala, India;* [3]*Research and Development Centre, Bharathiyar University, Coimbatore-641046, Tamil Nadu, India;* [4]*Bioinformatics Research Laboratory, Eminent Biosciences, Vijaynagar, Indore-452010, India;* [5]*In Silico Research Laboratory, LeGene Biosciences, Vijaynagar, Indore-452010, India;* [6]*Department of Biochemistry, PSG College of Arts and Science, Coimbatore-641 014, India*

Abstract: ***Background*:** Alterations in GABAnergic system are implicated in the pathophysiology of schizophrenia. Available antipsychotics that target GABA receptor form a desirable therapeutic strategy in the treatment regimen of schizophrenia, unfortunately, suffer serious setback due to their prolonged side effects. The present investigation focuses on developing QSAR models from the biological activity of herbal compounds and their derivatives that promise to be alternative candidates to GABA uptake inhibitors.

***Methods*:** Three sets of compounds were undertaken in the study to develop QSAR models. The first set consisted of nine compounds which included Magnolol, Honokiol and other GABA acting established compounds. The second set consisted of 16 derivatives of N-diarylalkenyl-piperidinecarboxylic acid. The third QSAR dataset was made up of thirty two compounds which were Magnolol and Honokiol derivatives. Multiple linear regressions (MLR) and support vector machine (SVM) supervised quantitative structure-activity relationship (QSAR) models were developed to predict the biological activity of these three sets. The purpose of taking three QSAR sets of diverse chemical structures but identical in their GABA targeting and pharmacological action was to identify common chemical structure features responsible for structure-activity relationship (SAR).

***Results*:** Linear and non-linear QSAR models confirmed that the three sets shared common structural descriptors derived from WHIM (Weighted Holistic Invariant Molecular descriptors), 3D-MoRSE and Eigenvalue classes.

***Conclusion*:** It was concluded that properties like electro negativity and polarizability play a crucial role in controlling the activity of herbal compounds against GABA receptor.

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1. INTRODUCTION

Over the past decade, much of the attention regarding the treatment for schizophrenia and related psychotic disorders has focused on a new class of antipsychotic medications. The therapeutic strategy for the treatment of schizophrenia has seen considerable growth in the past half century [1-4] by the advent of drugs targeting GABAnergic system which has marked the beginning of the pharmacologic era in psychiatry [5-7]. In spite of the tremendous progress that has been made in confronting the disease, the pharmacological properties that confer the therapeutic effects on GABAnergic system have remained elusive, and certain side effects can still impact patient health and quality of life [8]. In addition, the efficacy of antipsychotic drugs is limited prompting the clinical use of adjunctive pharmacy to augment the effects of treatment [9, 10]. Moreover, the search for novel GABAnergic antipsychotic drugs has not been successful to date, though numerous development strategies continue to be pursued [11].

Quantitative structure activity relationship (QSAR) has proved its usefulness in predicting the biological response of

*Address correspondence to this author at the Department of Biochemistry, PSG College of Arts and Science, Coimbatore-641 014, India; Tel: +91 9944641506; Fax: +91 4224270120; E-mail: victordoss64@hotmail.com

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