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IN SILICO IDENTIFICATION OF PUTATIVE ANTI-OBESITY COMPOUNDS FROM *HUNTERIA UMBELLATA* SEEDS

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Introduction

One of the major problems in the world is obesity. Currently, 39% of the global population is obese with evidence of several health challenges such as high blood pressure, dyslipidemia, diabetes, coronary heart disease, stroke, gallbladder disease, and others [1]. Although a few drugs such as orlistat, diethylpropion, benzphetamine, and sibutramine have been used to treat obesity however, most of the drugs come with adverse effects, including nausea, constipation, and pancreatitis [2]. Thus, creation of new drugs is crucial for improving patient outcomes and life's quality. In the stomach is the ghrelin hormone that acts at the ghrelin receptor in several bodily tissues. Ghrelin receptor agonists can improve body composition, and increase food intake and appetite [3]. *Hunteria umbellata* Seeds (HUS) has been reported to be effective against obesity in traditional medicine [4]. Nevertheless, this assertion has not been validated to understand the active compound responsible for this action. Using computer-aided drug design techniques, identification of the actual bioactive compound could be achieved. Therefore, this study employs an in silico technique to screen the phytochemicals in HUS to cognize the bioactive agent that plays a vital role in ameliorating obesity.

Methodology

The research started by downloading a ghrelin agonist receptor with ID: 7F9Y from a protein data bank. Homology modeling of the target was done via the Robetta server while the Computed Atlas of Surface Topology of proteins (Castp) algorithm was employed to identify the binding site with the grid center: x = -12.049 Å; y = 33.452 Å; z = -20.183 Å. Before docking, polar hydrogen and Kollman charges were added to the protein through the Autodock4 algorithm. Thirteen HUS phytochemicals were extracted from the literature [3] and prepared by adding polar hydrogen and Gasteiger charges. The docking process was achieved with Autodock vina. At the same time, the behavior of the protein-ligand complex was studied through a molecular dynamics simulation for 100 ns with Amber while pharmacokinetic properties were determined using the AdmetSAR server.

Our result shows that 2,2′-Benzylidenebis (3-methylbenzofuran), 2-Ethylacridine, 5-Methyl-2-phenylindolizine, and Urs-12-en-24-oic acid strongly and specifically bind to ghrelin receptor having inhibition constant (K_i) of 0.046, 1.50, 1.34, 0.046 μM, respectively. This is far better compared to some FDA-Approved anti-obesity medications especially orlisat, sibutramine, and benzphetamine with affinity of K_i = 10.23, 17.40, and 47.30 μM, respectively. Also, the absorption, distribution, metabolism, excretion, and toxicity (ADMET) screening further proves the efficacy of the bioactive compounds in terms of higher blood-brain and human intestinal permeability.

Conclusion

This study unveiled major anti-obesity compounds present in HUS. It was noticed that four compounds specifically outperformed some commercially available anti-obesity drugs based on their ligand-protein interaction and ADMET screening. Therefore, in vitro and in vivo methods are needed to validate the in silico perspective.

References:

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