Bioinformatics Approaches to Natural Product Discovery

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Introduction: Bioinformatics is a multi-disciplinary field that usually uses approaches in Computer Science such as algorithms and machine learning to solve problems in the domains of Biology, Biochemistry, and other domains involving molecular biology data. This approach can also be used to screen natural products that have certain properties. Jamu or Indonesian herbal medicine works with the principle of multi-component multi-target. This principle focuses on the complex interactions of system components that describe how multi-components (compounds) can work together to affect multi-targets (protein targets). This mechanism is also popularly called Network Pharmacology. In this study, we introduce a workflow to screen herbal compounds based on Network Pharmacology and machine learning approach. Methods: The workflow starts by screening for proteins that have an important role in relation to a certain disease. The screening was conducted by applying clustering and utilizing network topological features which were represented as graphs [1]. Furthermore, we performed enrichment analysis by integrating the protein-protein interaction network with the Gene Ontology (GO) network covering biological processes, molecular functions, and cellular components into k-partite graph and analyzing them using soft clustering method [2]. From the results of this enrichment analysis, we determined which proteins are really relevant and have important role in a certain disease [3]. Next, from these screened proteins, we built a predictive models of compound-protein interactions from drug data collected from the DrugBank and SuperTarget databases and train the models using machine learning or deep learning methods [4]. This model was then used to predict Indonesian herbal compounds from the HerbalDB database (http://herbaldb.farmasi.ui.ac.id/v3/) and IJAH Analytics. Results: To demonstrate the effectiveness of the workflow, we applied it to analize some diseases, such as hyperinflamation in Covid-19 and obesity. We found several potential plants such as *Andrographis paniculata* (Sambiloto) to reduce the inflammatory effect on Covid-19 and *Murraya paniculata* (Kemuning) to activate Brown Adipose Tissue (BAT) which has the potential to treat obesity. Certainly all of this requires proof through in vitro, in vivo, and clinical trials. We have also implemented several processes in the workflow into the IJAH Analytics application. Some of the features of IJAH are finding herbal compounds or plant formulas based on specific disease or protein targets; and otherwise looking for the efficacy of several combinations of plants or herbal compounds. In addition, IJAH Analytics can also visualize pharmacological networks from plants-compound-protein-diseases. IJAH is available to the public at https://ijah.apps.cs.ipb.ac.id for free. Conclusion: This study shows the potential of using bioinformatics approaches based on network pharmacology and machine learning in discovering the potential of natural products from Indonesia's biodiversity. In addition, IJAH Analytics, although still in the refinement stage, can be an alternative application that can support researchers to screen potential Indonesian natural products. Keyword: bioinformatics, jamu, machine learning, natural product, network pharmacology

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