SCREENING FOR LEAD COMPOUNDS AND HERBAL EXTRACTS WITH POTENTIAL ANTI-INFLUENZA VIRAL ACTIVITY

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Abstract. Nonstructural protein 1 (NS1) of the highly pathogenic avian influenza virus (H5N1) contains a conserved RNA binding domain (RBD) that inhibits antiviral functions of host-innate immune response. Dimerization of NS1 forms a central groove and binds to double stranded (ds) RNA. This region might serve as a potential drug target. In this study, three dimensional structure model of NS1 RBD protein was constructed and virtual screening was performed to identify lead compounds that bound within and around the central groove. The virtual screening showed that 5 compounds bound within the central groove with binding energy ranging between -16.05 and -17.36 Kcal/mol. Two commercially available compounds, estradiol and veratridine, were selected for using in an *in vitro* screening assay. The results showed that neither of the compounds could inhibit the association between dsRNA and NS1 RBD protein. In addition, 34 herbal extracts were examined for their inhibitory effects. Five of them were able to inhibit association between NS1 RBD and dsRNA in electrophoresis mobility shift assay. Four herbs, *Terminalia belirica, Salacia chinensis, Zingiber montanum* and *Peltophorum pterocarpum*, could reduce >50% of infectivity of H5N1 in a cell-based assay, and it is worth further studying their potential use as source of antiviral drugs.

Keywords: virtual screening, antiviral compounds, NS1 protein, influenza A virus, herbs

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