An In silico approach for the identification of GRB2 inhibitors for the treatment of Polycystic ovary syndrome (PCOS)

Anshika Agarwal\(^1\), Anuraj Nayarisseri\(^{1,2,*}\)

Corresponding author: anuraj@eminentbio.com; Tel: +91 9752295342

1. In silico Research Laboratory, Eminent Biosciences, Mahalakshmi Nagar, Indore – 452010, Madhya Pradesh, India.

Background:

Polycystic Ovary Syndrome (PCOS) is extremely prevalent and diverse. It is the most commonly encountered heterogeneous endocrine disorder in premenopausal (reproductive age) women worldwide.\(^1\) Studies shows that it affects 5-10% of this population.\(^2\) It is a characteristic syndrome of ovarian dysfunction associated with hyperandrogenism, chronic anovulation, endometrial hyperplasia and significant morbidity. Many other crucial body systems are also affected causing hirsutism, infertility, alopecia, menstrual irregularities and obesity.\(^3\) The aetiology of this syndrome is still debatable. Although it is found that PCOS is common among middle and high-income urban population rather than in the rural population.\(^5\) The women with PCOS have a higher risk of developing type 2 diabetes mellitus and impaired glucose tolerance at an early stage.\(^4\) Insulin resistance is the key feature of PCOS and it is characterised by hyperinsulinemia. Obese women are at a higher risk of developing insulin resistance than normal-weight women and have higher hyperandrogenism.\(^6\)

The growth factor receptor-bound protein-2 (GRB2) is an adapter protein and is essential for cellular functions. It can either promote or block the cellular transformation and proliferation depending upon its activation and inhibition respectively. It plays a critical role in linking cell surface growth receptors (EGFR) and the Ras signalling pathway.\(^7\)

It is very crucial to curb the overexpression of the protein by using a potent ligand to activate essential cellular functions. It is used to comprehend the strength of association and the binding affinity between the appropriate ligands and the target binding site. This helps to develop more efficient drug candidates which would essentially help in the curing of the syndrome. The aim of the present investigation is to identify a potential GRB2 inhibitor...
towards the clinical treatment of Polycystic ovary syndrome (PCOS) using various molecular docking\textsuperscript{[8-15]} and virtual screening approaches\textsuperscript{[16-28]}.

\textbf{Keywords:} Polycystic ovary syndrome (PCOS), GRB2, GRB2 inhibitors, Molecular Docking, Virtual Screening, ADMET.

\textbf{REFERENCES:}


