Identification of new leads for human IGFBP-2: a therapeutic target for cardiovascular diseases

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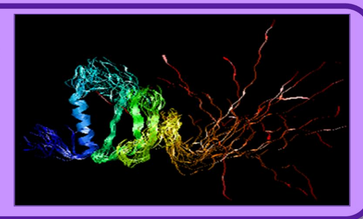
INTRODUCTION:

Human insulin like growth factor binding protein-2 is the largest member of insulin-like growth factor binding protein family. Human IGFBP-2 is present in circulation where it acts to prolong half life of circulating IGFs, peripheral tissues and also in biological fluids. Human IGFBP-2 is down regulated in various diseases like obesity, type II diabetes mellitus, which upon aging leads to heart stroke. Therefore, human IGFBP-2 was selected as a drug target for cardiovascular disease therapy. In the present study high-throughput virtual screening and molecular docking studies were used to identify novel leads that up regulate the activity of human IGFBP-2.



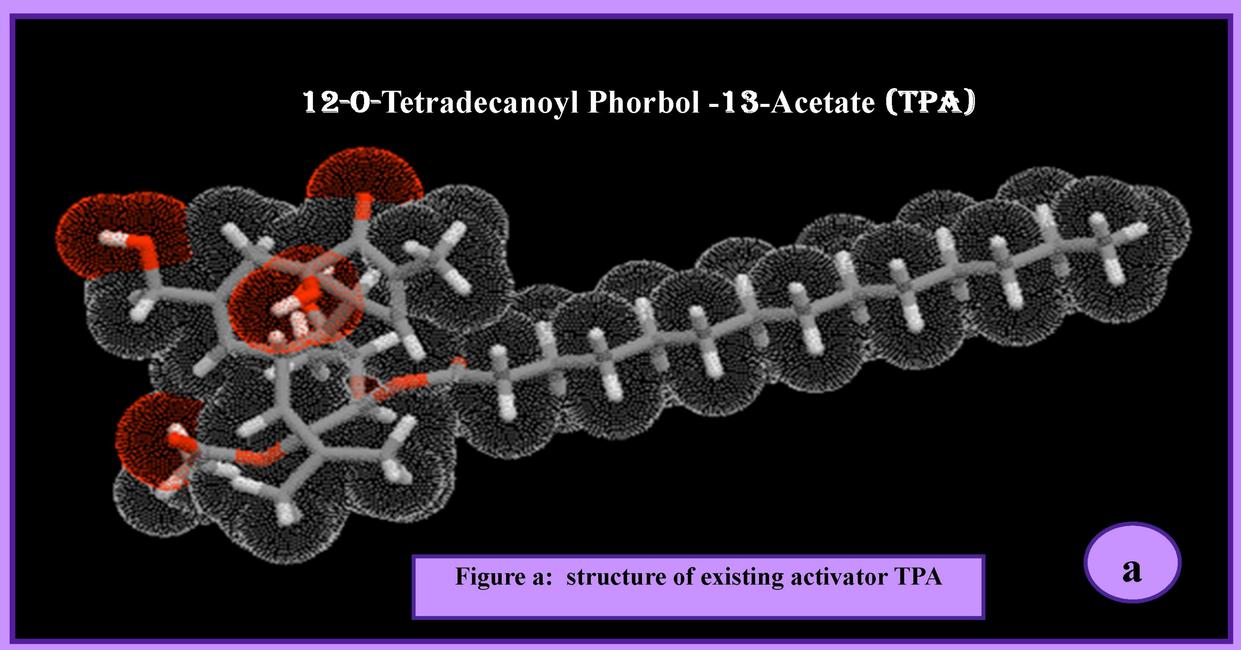


Figure a: structure of existing activator TPA

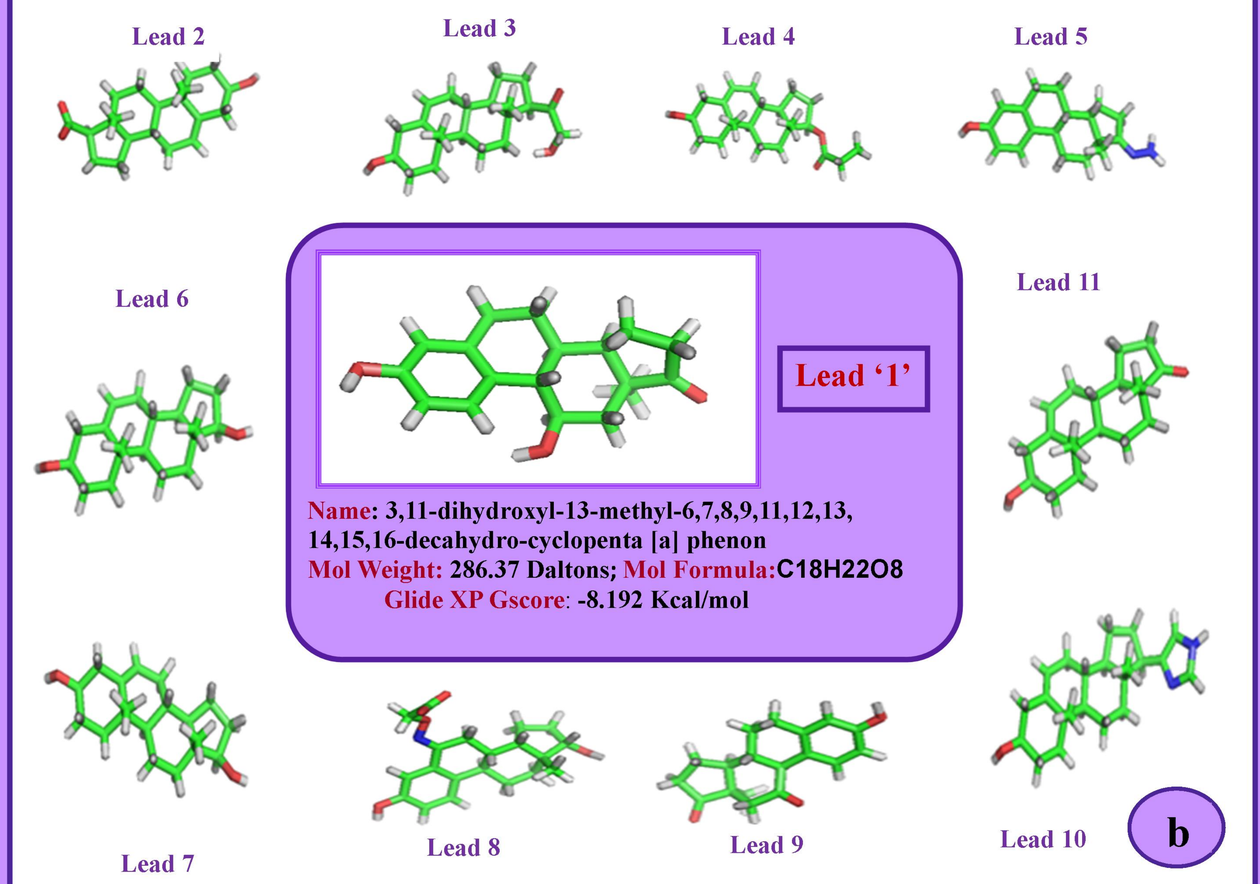


Figure b: Structures of proposed leads

MATERIALS AND METHODS

RESULS AND DISCUSSION

383 compounds → 1616 compounds

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Qik Prop → 1606 compounds

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Glide HTVS → 1008 compounds

↓

SP Docking → 151 compounds

↓

XP Docking → 35 compounds

↓

11 leads were selected

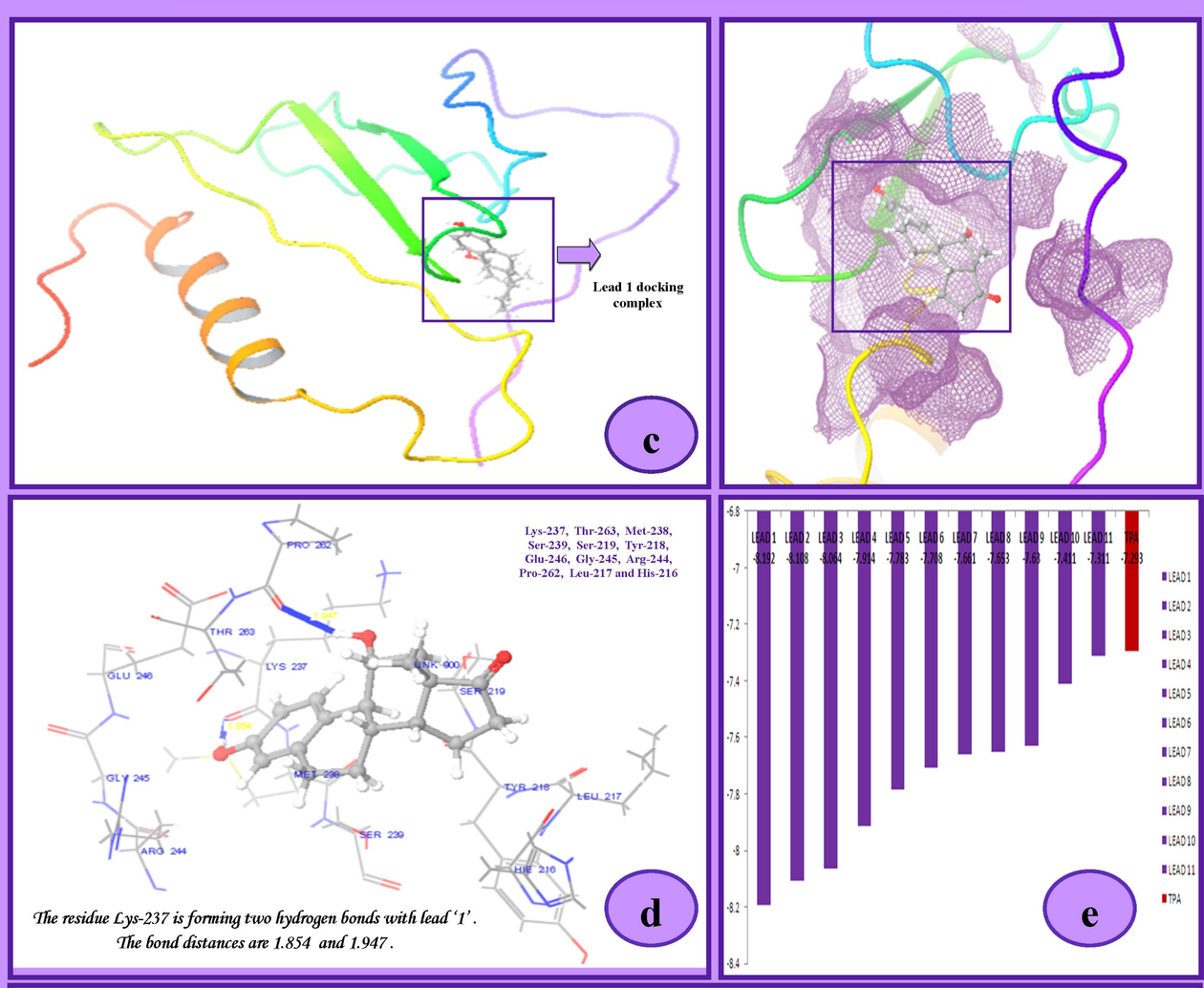

Figure c: *Docking complex of lead '1' with human IGFBP-2.* . Figure d: *Hydrogen bond network between lead'1' & human IGFBP-2.* . Figure e: *Comparison of docking scores between lead molecules & TPA activator*

CONCLUSION:

Low circulating levels of human IGFBP-2 leads to heart stroke.. Lead '1' 3,11-dihydroxyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-cyclopenta [a] phenon is having good pharmacological properties, better docking score and good binding affinity to human IGFBP-2 protein than the existing activator (TPA). Hence, lead '1' is proposed as a promising lead to elevate the activity of Human IGFBP-2 protein if synthesized and validated in animal models.

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