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Lead optimization of curcumin to enhance its pharmacokinetics and pharmacodynamics.

Abstract

Curcumin is a wonder molecule, the rare one to have multiple therapeutic effects with a plethora of molecular targets. Numerous reports suggest that curcumin has chemopreventive and chemotherapeutic affects but so far no definite single drug profile has been obtained with either curcumin or its derivatives/conjugates. Probably the problem lies with its less bioavailability, poor absorption, fast metabolism and non selective binding. To overcome these limitations several of its bioconjugates and analogs have been designed and tested. The present work involves *in-silico* lead optimization. Curcumin is being used as lead molecule to enhance its pharmacokinetic properties like solubility and partition coefficient. *In silico* lead optimization methods like combinatorial library design and docking based virtual screening are being used to increase its bioavailability and reduce toxicity. Pharmcodynamic features are considered by maintaining high binding affinity and selectivity using comparative docking approach. This structure based drug designing approach is directed to design and synthesize potent, selective and highly bioavailable curcumin based therapeutic agents. Out of 1527 analogs which were made *in-silico* ,few analogs show good ADMET(Absorption Distribution Metabolism Excretion Toxicity). We have found by docking studies that 4,4'-O-bis-glycinoyl and 4,4'-O-bis-tetra-glycinoyl derivatives bind much more strongly with human serum albumin than curcumin itself. These *in silico* results show good correlation with the wet lab studies.