Curcumin, A Potent Plant Ligand In Binding With BDNF, For Mitigating Type 2 Diabetes

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Abstract: *Type 2 Diabetes a fast growing health problems is influenced by a number of factors like genetic, personal and environmental factors. BDNF a potent Neurotrophin along with its receptor TrkB play an important role in influencing the signaling and insulin production pathways. SNPs on these molecules result in non binding of the two and decreased production of BDNF. Potent plant ligands can bind with BDNF and help in effective functioning of pathways. Curcumin a plant ligand from Curcuma longa exhibits an effective binding with BDNF and increases its levels in blood. The binding capacity was analyzed by docking analysis.*

Key Words: *Type 2 Diabetes, BDNF, Curcumin, docking analysis*

Introduction

Diabetes mellitus, is one of the most non-communicable epidemic diseases, the prevalence is increasing rapidly during the last three decades. According to the estimates of The International Diabetes Federation [IDF] (2017), the number of people with diabetes will rise to 629 million by 2045, indicating a 45% increase throughout the world. The T2DM is usually associated with relatively higher blood glucose levels and insulin resistance in several conditions. The etiology of T2DM is not well understood, but it may be related to genetic, personal and environmental factors. Diabetes Mellitus is strongly associated with micro and macro vascular complications More than 50 percent of patients with diabetes are affected by either diabetic Retinopathy, diabetic Neuropathy and diabetic Nephropathy [2].

Neurotrophins are potent molecules which protect and promote the growth and development of nerves. They have effects on neuronal differentiation, survival, neurite outgrowth, synaptic formation, and plasticity. In the central nervous system (CNS), Brain-derived Neurotrophic factor (BDNF) and its high-affinity receptor TrkB are highly expressed in the hypothalamus, where this Neurotrophic factor has major regulatory roles in the control of appetite and metabolism[3] and is a potential therapeutic target in numerous neurological, mental and metabolic disorders[4].In mammals, BDNF and TrkB are highly produced and released in several hypothalamus and hippocampus nuclei and known to be involved in glucose and energy homeostasis [5].

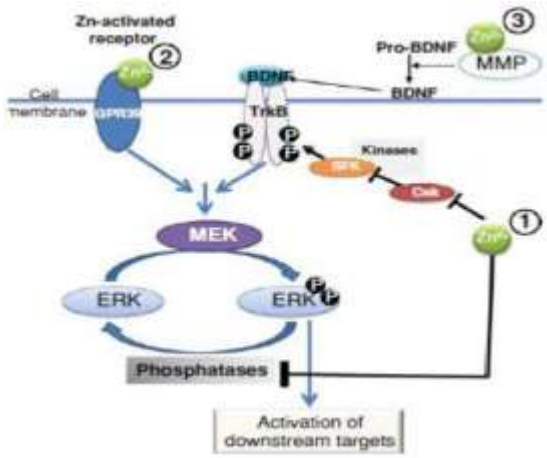


Figure 1: BDNF –TrkB interactions

Mutations (SNPs) on any of these two molecules would result in improper or non bonding of the two, which would lead to imbalance and interruption in a number of pathways, like signaling and glucose metabolism etc. This in turn may lead to the onset of Type II Diabetes, which would be clearly indicated by a fall or decrease in BDNF levels in blood.

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity because of their natural origin and less side effects. Many of the traditional medicines are derived from medicinal plants, minerals and organic matter [6]. Natural products have received considerable attention for the management of diabetes and its complications [7]. The spice turmeric, which is derived from the rhizomes of the plant Curcuma longa, has been described as a treatment for diabetes in Ayurvedic medicine.

Various studies indicate that Curcuminoids intake (1,500 mg/day) for 6 months continuously increased insulin sensitivity, decreased pulse wave velocity, triglyceride level, and atherosclerosis incidence in patients with T2DM, indicating that curcuminoids supplementation could contribute to a lower risk of cardiovascular events in dyslipidemic patients with T2DM.

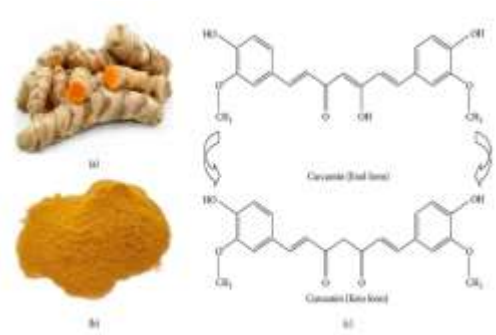
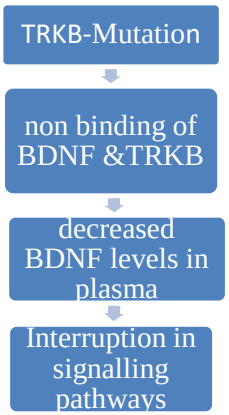


Figure 2: The molecular structure of Curcumin isolated from the root of turmeric. Curcumin, a natural compound, is the most active agent of the polyphenolic curcuminoids derived from the root of turmeric (Curcuma longa).

Discussion: Mutation in TrkB hinders the binding of BDNF and TrkB which causes a decrease in mature BDNF levels in the blood. According to the above performed docking results, Curcumin can substitute or mimic TrkB. Hence in a person with mutated TrkB, the series of affects may be as follows:



The present study involves docking of plant ligands called Curcuminoids with BDNF as a substitute of TrkB, in turn elevating the BDNF levels in blood. The binding capacity of Curcumin was checked and analyzed with BDNF using docking studies. Binding of BDNF with Curcumin was done. A comparison of binding energies of BDNF-Curcumin were done. These binding energies indicate a good bonding.

As indicated earlier in a number of publications and literature survey. Curcumin which is a potential plant ligand present in the rhizomes of Turmeric (Curcuma longa) helps in elevating the plasma BDNF levels as well as plays an

important role in controlling the blood sugar levels. The same has been proved by the docking results which has been performed using Swiss dock online software.

◉	42	0	-709.85	-5.74
○	43	0	-708.63	-6.23
○	43	1	-706.56	-6.46
○	43	2	-706.19	-6.45
○	44	0	-708.42	-6.16
○	44	1	-708.03	-6.08
○	44	2	-708.03	-6.08
○	44	3	-707.67	-6.08
○	44	4	-707.67	-6.08
○	45	0	-707.37	-6.73
○	46	0	-707.24	-6.12
○	46	1	-700.84	-5.96
○	47	0	-706.86	-6.18
○	48	0	-706.55	-6.64
○	49	0	-706.50	-6.15
○	50	0	-706.40	-6.84
○	51	0	-706.16	-6.27
○	52	0	-706.02	-6.09
○	53	0	-705.04	-6.12
○	54	0	-704.28	-6.08
○	55	0	-702.83	-5.88
○	56	0	-702.02	-6.00
○	57	0	-697.47	-6.02
○	57	0	-697.47	-6.02

Figure 3:BDNF-Curcumin

Conclusion: Curcumin binds with BDNF and causes increased BDNF levels. The above analysis shows the bonding of BDNF and Curcumin is good at the 45thposition. Hence further structural studies can modify or create a new drug using Curcumin. The above conclusion has been drawn after comparing few plant ligands & their bonding capacity with BDNF.

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