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Research Article

NATURAL PRODUCT-BASED AMYLOID PROTEIN INHIBITORS

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ABSTRACT

Neurodegenerative disorders like Alzheimer's are associated by plague formation of protein aggregates called amyloid proteins. Many natural-based products such as flavonoids, phenolic acids, iso-flavones, and polyunsaturated fatty acids play major role in therapeutic ability to degrade, slow down, and recondition the amyloid protein (amyloid protein inhibitors). These compounds extracted from plants have shown consequential potential in *in vitro* studies as well as *in vivo* studies. For requisite for brain nutritive growth, omega 3 fatty acids are important, whereas ß-carotene plays indispensable role in cognitive impairment and oxidative stress in the brain. It is described that omega 3 fatty acids are extracted from the source (flaxseed) by oil press method and ß-carotene is synthesized by physiochemical process from carrot. The main objective of this particular research topic is to provide more effectiveness in detaining the growth of amyloid protein inhibitors in brain. It is observed that the product with omega 3 and ß-carotene slow down the protein aggregation more efficiently than omega 3 capsules alone and intra-cerebroventricular injected streptozotocin. This can be determined by *in silico* activity of acetylcholinesterase. The analyses show extensive reciprocity between inhibitors and amyloid proteins. The administration of omega 3 with ß-carotene depreciates the amyloid protein aggregates more efficiently. Hence, it is suggested that the product can be used as treatment for neurodegenerative diseases like Alzheimer's.

Keywords: Beta-carotene, Omega 3 fatty acids, Amyloid protein inhibitors.

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INTRODUCTION

Numerous constant human infections, including different neurodegenerative sicknesses, are related with harmful protein totals, additionally known as β-protein amyloids. One normal restorative system is to enhance protein collection inhibitors which may back off, forestall, or redesign poisonous amyloid [1]. Regular items are a significant type of amyloid inhibitors, and a few many characteristic item relevant amyloid inhibitors have been distinguished and portrayed lately. These plant- or microorganism-extricated mixes have indicated noteworthy remedial effectiveness from *in vitro* investigations just as *in vivo* creature tests. In spite of the specialized difficulties of inborn disarranged or halfway unfurled amyloid proteins that are less manageable to portrayals by basic science, a lot of exploration has been undertaken, yielding biochemical and pharmacological bits of knowledge into how inhibitors work [3]. This survey expects to sum up late advancement in characteristic product relevant amyloid inhibitors and further to dissect the components of restraint *in-vitro* [2]. Significant types of normal item liability and in what manner they are distinguished are portrayed. The examinations extensively portray the atomic connections among the inhibitors and pertinent amyloidal proteins. Such connections are depicted at sub-atomic and nuclear extent, which incorporate covalent, metal, and non-covalent interceded components. *In vivo* creature considers and clinical preliminaries are summed up as augmentation. To improve common item bioaccumulation *in vivo*, rising study utilizing nanocarriers for conveyance are additionally been portrayed.

Some examples for natural product-based amyloid protein inhibitors [8]

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METHODS

A few plant-inferred characteristic mixes are known to show resistance against amyloid conglomeration movement that makes them appealing as expected treatments to cure Alzheimer's disease (AD's) (Alzheimer's) illness. This system of enemy of amyloidal movement was not notable. Moreover, in such manner, numerous characteristic mixes are believed to exhibit pro-founding authoritative to different amyloidal species along with fibrils and oligomers that may prompt configurational change in the β-sheet gathering to shape non-toxic

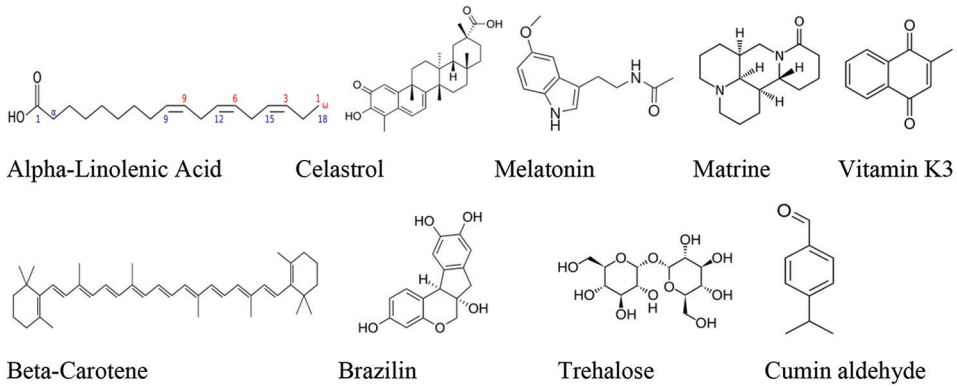
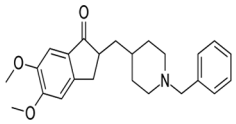
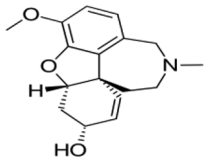
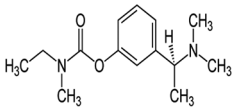
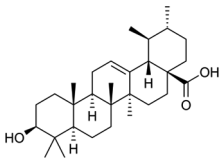


Table 1 : Some currently used drugs for Alzheimer's [9]

Brand name	Chemical Composition	Molecular Formula	Side effects
Donepezil (Aricept)		$C_{24}H_{29}NO_3$	Aggression, feeling tired, trouble sleeping, nausea, and diarrhea
Galantamine (Razadyne)		$C_{17}H_{21}NO_3$	Nausea, vomiting bradycardia (slow resting heart rate)
Rivastigmine (Exelon)		$C_{18}H_{28}N_2O_8$	Nausea, vomiting, intense itching, redness, swelling, and skin rashes
Memantine (Namenda XR)		$C_{12}H_{21}N$	Headache, constipation, sleepiness, and dizziness
Ursodeoxycholic acid (Destolit)		$C_{30}H_{48}O_3$	Diarrhea, pasty stools, and nausea

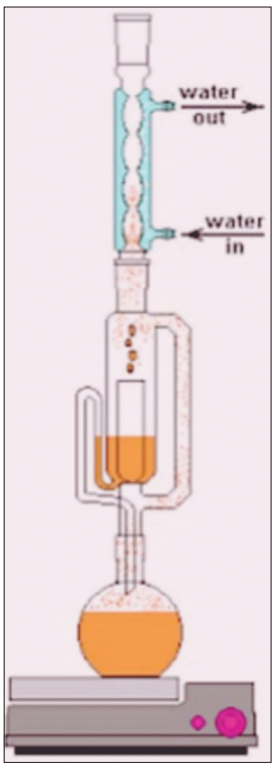


Fig. 1: Soxhlet apparatus to extract beta-carotene [12]

totals [6]. The survey examines an instrument of hostile to amyloidal action of about 16 characteristic mixes and provides auxiliary subtleties on the immediate restricting collaborations with amyloidal totals. The topographical examinations depict that the alchemy behavior of regular items does accommodate standards of Lipinski and also that catechol and catechol-type moieties occur in common mixes go about

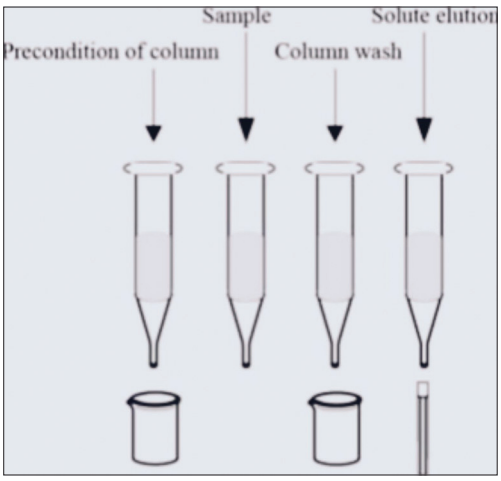


Fig. 2: Solvent extraction to remove impurities [13]

as in lysine's site explicit liability of amyloidal collection [7]. In light of these perceptions, we propose an auxiliary layout to plan novel little atoms including site explicit oval platforms, planar fragrant, and non-aromatic substitutes with reasonably subbed hydrogen bond acceptors and contributors [20]. These investigations will be having huge ramifications in this plan and advancement of novel amyloidal accumulation liability along with unrivaled metabolic steadiness and blood cerebrum hindrance infiltration such as expected specialists to diagnose AD's ailment.

Role of beta-carotene and omega 3 fatty acids

Natural products can degrade the amyloid plagues more effectively. Beta-carotene which is extracted from carrot and omega 3 fatty acids from flaxseed slow down the growth of amyloid plagues [8,13]. In some cases, the AD patients are treated with omega 3 fatty acids drink fish. It has more effectiveness in reducing the symptoms of

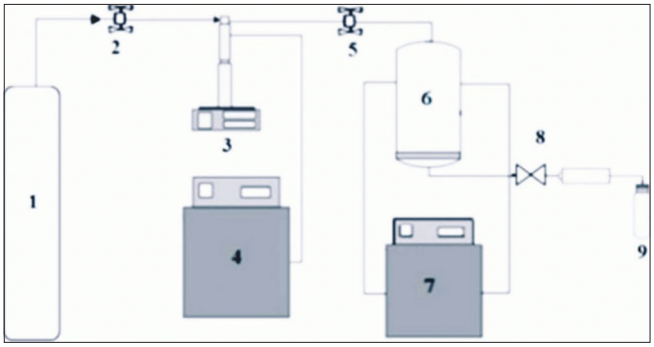


Fig. 3: Propane oil extractor [17]. (1) Propane cylinder, (2, 5) needle valves, (3) high pressure pump, (4, 7) thermostatic bath, (6) extractor, (8) micrometric expansion valve, (9) flaxseed oil collector.

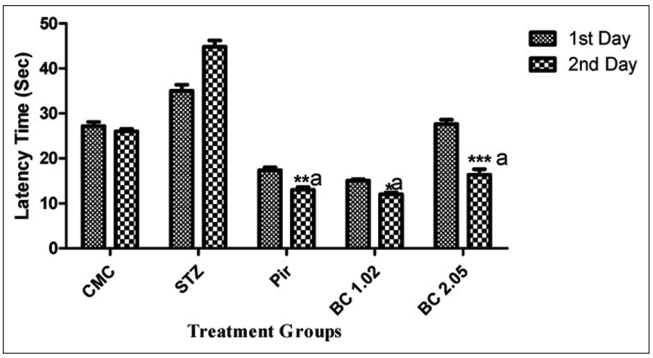


Fig. 4: Impact of beta-carotene on transfer latency using the model of elevated plus maze in animals (mice) which has received streptozotocin. The data are represented in terms of mean n=10, ±SEM, p<0.05. Importance is given to diseased group comparison and p<0.05*, 0.01, and 0.001*** were described with the count of day 1. Pir: Piracetam, STZ: Streptozotocin, BC: Beta-carotene**

dementia [8]. Docosahexaenoic acid corrosive (DHA), the significant omega 3 unsaturated fat in neurons, has lay hold off on a focal function as an objective for helpful mediation in Alzheimer's sickness (AD). A plenty of *in vitro*, creature model, and human information, assembled over the previous decade, feature the significant job DHA may play in the advancement of an assortment of neurological and mental problems, including AD. Beta-carotene can be synthesized by Soxhlet method and omega 3 fatty acids can be extracted using propane oil extraction method.

Extraction and synthesis of beta-carotene

The apparatus is a little more advance than the reflux boiling equipment. Between the condenser and the round bottom flask containing the solvent, a Soxhlet extractor containing a chamber carrying a "thimble," made of thick filter paper, packed with the solid to be extracted, and is placed [11]. The solvent is heated to reflux, the vapor travels through the passage of the extractor, and the condensate drips back down into the solid material. The solvent fills up the chamber while the material is extracted from the solid. When the solvent volume has almost filled the chamber, the solvents containing the extract flows back into the round bottom flask through a siphon tube [12]. The process is repeated for a number of cycles and the extract is accumulated in the round-bottom flask. Running the extraction for a prolonged period may extract material that is only slightly soluble in the solvent.

Detection method

Solid-phase extraction column (50 mg) is used. This procedure includes steps as follows: 1–3 ml methanol is added for precondition. A small amount of the sample is placed on the column, then methanol is used

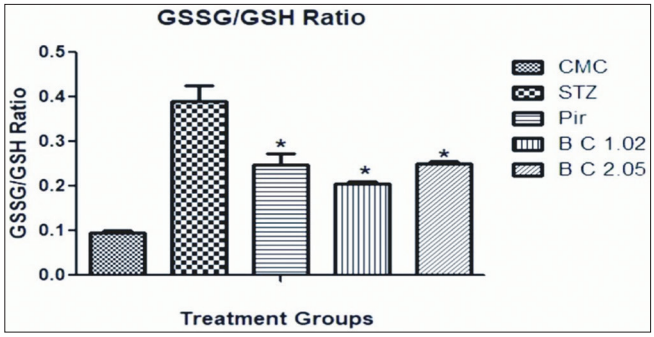


Fig. 5: Impact of beta-carotene in the progression of latency using the passive avoidance model in animal (mice) which have received streptozotocin. The data are depicted in the form of mean n=10, ±SEM. Importance is given in diseased group comparison. p<0.001 is given importance to diseased group

to wash the column and gradually the β-carotene is eluted by methyl tertiary butyl ether [13].

Extraction of omega 3 unsaturated fatty acids using propane oil extraction

The flaxseed powder is placed inside a hard aluminum barrel-shaped chamber in-between two cotton layers to keep the particles away from impeding the framework of the extraction [20]. The temperature of the extraction is constrained by a thermostatic shower and furthermore to manage the pressurizing siphon temperature [15]. The steam rate of the propane in framework is physically constrained by a valve (micrometric). The volume of expended propane is determined using a pressurized siphon. The observed temperatures for extraction are 20°C, 40°C, and 60°C. The dissolved was siphoned at a steady steam rate (2 ml/min) into the chamber. The removed oil portions were collected at a rate (0, 3, 6, 10, 15, 20, 30, 40, 60, and 90) min and the addition of each and every individual part is hydrometrically decided for yield [16]. The yield of flaxseed oil is predicted by the composition by the measure of oil extracted to the measure of seed in the extractor. The extractions were acted in 3-fold [17].(1) Propane cylinder, (2, 5) needle valves, (3) high pressure pump, (4, 7) thermostatic bath, (6) extractor, (8) micrometric expansion valve, (9) flaxseed oil collector.

RESULTS AND DISCUSSION

The impact of beta-carotene on transfer latency by utilizing the elevated plus maze model of mice which was injected by streptozotocin

The elevated plus maze paradigm explains the cognitive performance. On the 15th day, animals were put through transfer latency evaluation. It is clearly determined that the animals which have received beta-carotene (1.02 mg/kg and 2.05 mg/kg) have shown very compelling value (p≤0.001) of transfer latency when compared to diseased mice group [18].

Impact of beta-carotene on the progressive latency using the model of passive avoidance in mice which has received streptozotocin

The long-term memory has been examined using the passive avoidance model based on progressive latency. Fig. 5 has clearly described that the mice which were treated with beta-carotene (1.02 and 2.05 mg/kg) have shown rather compelling (p≤0.01) enhancement in cognitive performance.

CONCLUSION

It is concluded that β-carotene and omega-3 fatty acids together work effectively against other synthetic drugs like streptozotocin. The effectiveness in work is explained by scanning electron microscope (SEM) and transmission electron microscope (TEM) graphical representation. The above graphical representation is SEM and TEM images of effectiveness of β-carotene and streptozotocin. B-carotene is proved to degrade amyloidal proteins. The graphical representation

shows that beta-carotene and omega 3 fatty acids effectively decrease the amyloid protein concentration. This degradation of β-amyloid plaques is possible at the early stage of the disease. The capsule can be also taken to prevent the buildup of β-amyloid plagues. The extra feature of the capsule is omega fatty acids are prepared from vegan source. Together both β-carotene and omega 3 fatty acids prove effectively against β-amyloid protein plagues.

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