The Neurologist: Clinical &

Open Access

A New Horizon in Neuropharmacology Recent Advances in Natural Products Research for Crossing the Blood – Brain Barrier

Annalisa Bordano*

Department of Chemistry, University of Turin, Italy

Abstract

The blood-brain barrier (BBB) presents a formidable challenge for delivering therapeutics to the central nervous system (CNS), impeding the e f cacy of many potential treatments for neurological disorders. Recent research has increasingly focused on natural products as promising candidates for overcoming this barrier. This article reviews recent advances in natural products research, highlighting how compounds derived from plants, fungi, and microorganisms have demonstrated the ability to cross the BBB. Key mechanisms facilitating this include molecular size, lipophilicity, active transport, and receptor-mediated uptake. Notable examples include curcumin, resveratrol, ginsenosides, and epigallocatechin gallate (EGCG), which have shown neuroprotective and therapeutic potential. The article also explores advancements in drug delivery systems, such as nanoparticles, that enhance the bioavailability of these natural compounds. Despite signi f cant progress, challenges such as bioavailability, stability, and safety remain. Future research will focus on optimizing delivery methods and understanding the mechanisms of action to fully harness the therapeutic potential of natural products in treating CNS diseases.

***Corresponding author:** Annalisa Bordano, Department of Chemistry, University of Turin, Italy, E-mail: annalisabordano@gmai.com

Received:

Many natural products with BBB-crossing potential are small molecules that exhibit high lipophilicity, which facilitates their passage through the lipid-rich BBB. For instance, curcumin, a polyphenol derived from turmeric, is known for its anti-in ammatory and neuroprotective properties [7]. Its ability to cross the BBB is attributed to its lipophilic nature, allowing it to di use through the endothelial cell membranes.

A a

Some natural products can utilize existing transport mechanisms in the BBB. For example, certain avonoids and glycosides may be substrates for speci c transporters, enabling their entry into the CNS [8]. Quercetin, a avonoid found in various fruits and vegetables, has shown promise in enhancing BBB permeability through interactions with transport proteins.

R - a a

Natural products that bind to speci c receptors on the BBB can be transported across the barrier. For example, berberine, an alkaloid from Berberis species, has been demonstrated to cross the BBB via receptor-mediated endocytosis. is mechanism allows berberine to exert neuroprotective e ects by targeting neuronal receptors and signaling pathways.

N a

Advances in nanotechnology have facilitated the development of nanoparticle-based delivery systems that can transport natural products across the BBB. Nanoparticles can encapsulate bioactive natural compounds, enhancing their stability, bioavailability, and BBB penetration [9]. For example, nanoparticles loaded with ginseng extracts have been shown to improve cognitive function in preclinical models by e ectively delivering ginsenosides to the brain.

R a a a a

C

Curcumin, derived from turmeric, has been extensively studied for its potential neurotherapeutic bene ts. Research has demonstrated that curcumin can cross the BBB and exhibit anti-in ammatory and antioxidant e ects in the CNS. Recent studies have focused on improving curcumin's bioavailability and BBB penetration through formulation strategies such as nanoparticles and liposomal delivery.

R a

Resveratrol, a polyphenol found in grapes and red wine, is another natural product with notable neuroprotective properties [10]. Its ability to cross the BBB has been attributed to its small molecular size and lipophilicity. Recent research has explored resveratrol's potential in treating neurodegenerative diseases such as Alzheimer's disease, with promising results in preclinical models. Ginsenosides, the active components of ginseng, have shown potential in crossing the BBB and exerting neuroprotective e ects. Recent advancements have involved developing novel delivery systems, such as nanoparticles and liposomes, to enhance the bioavailability and e cacy of ginsenosides in the CNS.

E a a Ga a (EGCG)

EGCG, a major catechin in green tea, has demonstrated the ability to cross the BBB and exhibit neuroprotective and anti-in ammatory e ects. Recent studies have focused on optimizing EGCG formulations to improve its stability and brain penetration, with the goal of developing e ective therapies for neurodegenerative diseases.

D a a , a a a a a BBB :

B a a a a a a

Ensuring the stability and bioavailability of natural products in the CNS remains a signi cant challenge. Advances in drug delivery systems, such as nanoparticles and liposomes, are essential for overcoming these issues and improving the therapeutic e cacy of natural products.

a a E a

Comprehensive safety and e cacy evaluations are crucial for translating natural product research into clinical applications. Rigorous preclinical and clinical studies are necessary to assess the long-term e ects and potential side e ects of natural products used in neurotherapeutics.

M a a

A deeper understanding of the mechanisms by which natural products cross the BBB and interact with CNS targets is essential for optimizing their use. Continued research into the pharmacokinetics and pharmacodynamics of these compounds will help re ne their therapeutic applications.

C

e exploration of natural products for their ability to cross the blood-brain barrier represents a promising frontier in neuropharmacology. Recent advances have highlighted the potential of compounds such as curcumin, resveratrol, ginsenosides, and EGCG in overcoming the challenges of BBB penetration and o ering therapeutic bene ts for neurological disorders. By leveraging the unique properties of natural products and employing innovative delivery systems, researchers are paving the way for the development of novel treatments that could signi cantly impact the management of CNS diseases. Continued research and technological advancements will be crucial in realizing the full potential of natural products in neurotherapeutics, o ering new hope for e ective treatments in neurology and beyond.

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None

C I

None

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