AYUSH: International Research Journal of Ayurveda Teachers Association

Journal Home Page: www.airjata.org

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Review Article

Title of Article:
A Critical Study of Ayurvedic Formulations On blood-Brainbarrier

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Article Info:

Article History:
Received: 30 january 2023
Accepted: 21 march 2023
Published: 1 april 2023

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ISSN No.: 2583-5971

ABSTRACT

The brain is the center of major neurological and psychiatric disorders.Brain blood capillaries have certain anatomical adaptations which act as physiological barriers. This limits the entry of molecules intothe brain. This is the stumbling block in delivering drugs acrossthe blood-brain barrier and a challenge to chemists globally in treating brain disorders. In Ayurvedic classics,there are formulations and treatment procedures which has a separate entity in treating brain disorder.

INTRODUCTION

Blood-brain barrier is a small but seriousimpediment of blood microvasculature inthe brain. This barrier separates blood fromthe extracellular fluid in the central nervous system.Hence the most formidable gatekeeper of the brain which impedesand regulates the entry of compounds fromthe blood to the brain and back.

Discovery In1885 Paul Ehrlich, a German bacteriologist injectedaniline dye intravenously whichcaused the staining of all organs except the brain. Edwin Goldmann in 1931[1], injected dye into the CSF directly,and the brain got stainednot the body, which helped in clearly understanding the existence ofthe haematoencephalic barrier.By the invention of Electron microscopy in 1960, it was found that the outermost layers of endothelial cells in brain capillaries were fused together. Thus blood brain barrier was proved to exist.

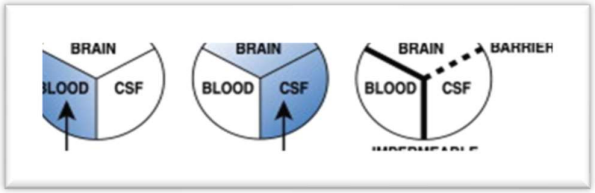
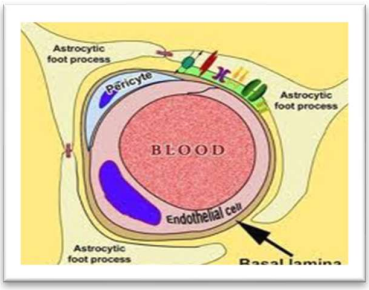


Fig.no.1: Discovery Of Bbb

Anatomy



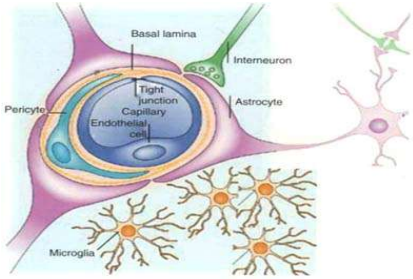


Fig.no2: cross section of brain capillaries

The double layer barrier was formed by endothelial cells with tight junctions, foot process of astrocytes and pericytes with basement membrane

Blood Supply

Brain is of only 2.5% of body weight, but 1/6th of entire cardiac output supplies to brain[2].Major arterial supply is by internal carotid anteriorly and vertebral arteries posteriorly forming circle of Willis and venous drainage from brain is through Dural sinuses.

Neurons are functional unit of nervous system and neuroglial cells are not neuronal cellular elements of nervous system. They provide support and protection for neurons. Functions of glial cells were foundto surround neurons and hold them in space and to supply nutrients and oxygen and isolate one neuron from others, also destroy pathogens and remove dead neurons.

Astrocytesarestar shaped glial cells ofcentral nervous system. Astrocytespick glucose from blood and provide nutrition to neurons.They provide biochemical support for Bloodmicrovascularendothelial cells [BMEC]. Factors released by astrocytes involve in postnatal maturation of Blood brain barrier.Thus direct contact between endothelial cells and astrocytes are necessary to generate Blood brain barrier. They act as a circuit or pathway to transmit information.

Pericytes

Mesenchymal like cells that have the power of contraction on blood vessels.It provides structural and vasodynamic capacity to microvasculature.It plays important role in structural integrity and genesis of Blood Brain Barrier.It hasphagocytic activity.Their functions are in two ways, by regulating blood brain barrier specific gene expression and by inducing polarization of astrocyte end feet surrounding blood vessels of central nervous system

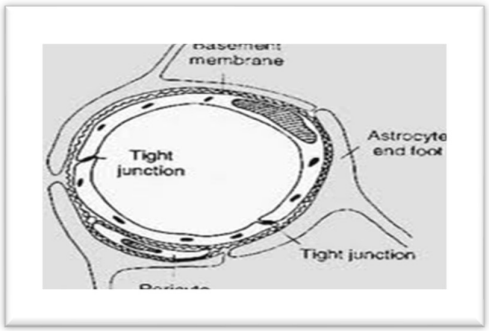


Fig.no 3: Tight Junctions

Tight junctions are thefusion betweenouter leaflets of plasma membrane of endothelial cells.They areformed by protein components likeClaudin,Occludin, Junction adhesion molecules and accessory proteins. In normal endothelial cells there isfenestrated gap junctions. Hence there is free passing of drug molecule in and out. In blood microvascular endothelial cells [BMEC] of brain is non fenestrated without gap junction.

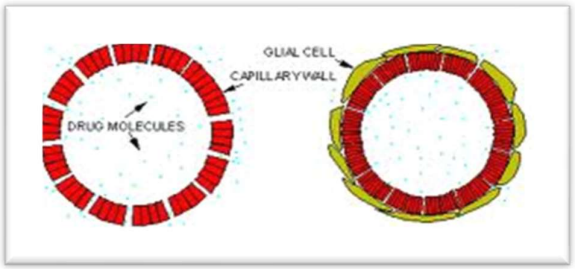


Fig. no 4: Endothelial Layer In Normal Blood Vessel & Bmec

Using*murdhini tailas*in the treatment procedures such as*pichu,dhara,abhyanga* and *shirovasthi;* is a separate entity in treating neurological disorders[3]. Probable mode of this action can theoretically be interpreted as drug enters through hair follicles into the superficial vessels in the scalp; these vessels areconnected to superior sagittal sinus of the brain by emissary veins, these emissary veins pass through parietal and occipital foramina of skull.
Five layers of scalp showing connection of superficial vessels and superior sagital sinus by emissary veins

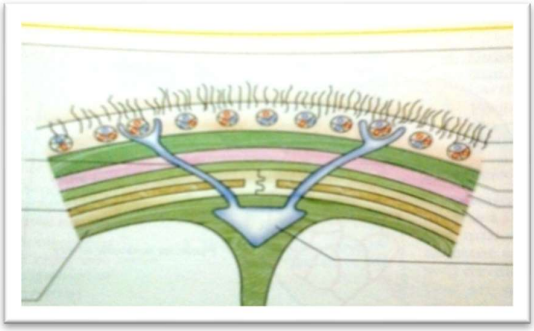


Fig.no. 5 Cadaveric picture showing parietal and occipital foramina

Circumventricular organs

Organs without blood brainbarrier includes Area postrema,Median eminence,Neurohypophysis, Pineal gland, Subfornical organ and Lamina terminalis.They are regions which need to respond to factors present in systemic circulation. These regions are isolatedfromthe remaining part ofthe brain by specialized ependymal cells called tanycytes.

Physiology

Blood-brain barrier blocks all molecules except those that cross cell membranes by means of lipophilic,hydrophobic nature(oxygen, carbondioxide,ethanol and steroid hormones). Those that are allowed in by specific transport systems (including sugars and some amino acids) regulate passage of ions in the blood .Substances having molecular weight higher than 500 daltonsgenerally cannot cross the Blood Brain Barrier. Hormones generally do not penetrate the brain except at the circumventricular organs. This protects the brain from common infections but viral infections do pass blood brain barrier. As antibodies are too large to cross the blood-brain barrier, infections are very serious and difficult to treat.Prevents endogenous and exogenous toxins in the blood entering tobrain.Prevents escape of neurotransmitter from brain back to blood

Factors Breaking Blood Brain Barrier

Hypertension, not fully formed at birth, hyperosmolality of urea, ammonia, etc, Microwaves, Radiations, Infections, Trauma and inflammation.

Drug Delivery Mechanism

This barrier hinders the delivery of diagnostic and therapeutic agents in to the brain. Mechanisms for drug targeting the brain involve going either "through"or "behind"the Blood Brain Barrier.Modalities for drug delivery through this mechanism, entail disruption of the Blood Brain Barrier by osmoticmean, biochemicallyby the use of vasoactive substances such as bradykinin and by localized exposure to ultrasound**.** Strategies for drug delivery behind the Blood Brain Barrier include intracerebral implantationor by direct physical injectionto the site of interest[4].Drug delivering across the Blood Brain Barrier is the most promising application of nanotechnology in clinical neuroscience.Nanotechnology helps in the transfer of drugs across the Blood Brain Barrier.Recently researchers have been trying to build nanoparticles loaded with liposomes to gain access through the Blood Brain Barrier**.**

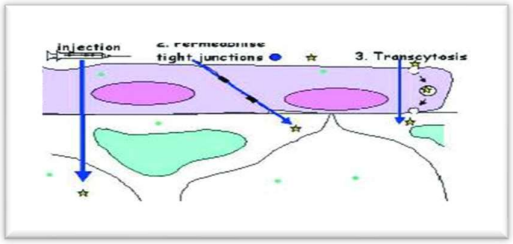


Fig.No. 6

Drug Delivery Mechanism

Mannitols arehexa hydric alcohol in plants readily pass Peptides-cross Blood Brain Barrier

Ayurvedic Outlook

In the present era, stress and changes in life style leads to break down of BBB.Though BBB has neuroprotective role,overcoming the difficulty in delivering therapeutic agent to specific site ofbrain presents a major step forward in treatment of neuropsychiatric cases.*Acharya Susrutha* says brain as *majja dhathu* in *shiras*[5]**.**70% of brain tissue consists of fat so a refined fat substance processed with herbs *(snehakalpana)such asBrahmi, Vacha, Sankhapushpi,Yashtimadhu,*and also *Swarna* etc will support functioning of brain and prevent functional deterioration.*Yashtimadu* is given with *ksheera,* beauty of *anupana* making the drug more lipophilic in nature, this

synergistic action will help to reach the drug at the intended site. In classics *acharyas* mentioned more *ghritha* and *taila kalpanas* as *bahya* and *abhyanthara prayoga* in major neurological and psychiatric disorders.Nasal medication or *nasya* has direct access to CNS as it passes Blood Brain Barrier. Rasa preparation readilypasses Blood Brain Barrier. Alcohol readily passes Blood Brain Barrier.*Aristas* and *asavas* contain selfgenerated alcohol that helps in quick absorption and assimilation by crossing Blood Brain Barrier.Ayurveda had mastered the art and science of nanoparticle development,centuries ago, when the whole worldwas still in dark about this wonderful phenomenon..Herbomineral formulations of ayurveda constituting *bhasma* as an ingredient are superior as it is even today.

In a nutshell, the Blood Brain Barrier and its chemistry shows that how ayurvedic drugs protects brain.

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How to cite article:

Archana Radhakrishnan, Manju P S. A Critical Study of Ayurvedic Formulations Onblood-Brainbarrier. AYUSH: International Research Journal of Ayurveda Teachers Association. 2023;2(1)15-18.