REVIEW OF PHYTOSOME POTENTIAL OF GOTTU KOLA (CENTELLA ASIATICA) EXTRACT TO RESTORE NERVE CELL MEMBRANE AND IMPROVE COGNITIVE FUNCTION

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ABSTRACT

One of the herbs in Indonesia, Gotu Kola (Centella asiatica) contains triterpenoid glycosides, which are ethnomedicine used as neuroprotectors. Phytochemical components of Gotu Kola extract tend to be polar, so it needs an approach to modify the polarity of the extract. The method is to formulate an extract in the form of phytosome as an herbal delivery system so that it can increase the absorption and bioavailability of the active substance. It is suitable for the delivery system of active compounds from plants because it can carry hydrophilic and lipophilic compounds from plants. This paper specifically reviews the potential of the plant extracts for the recovery of nerve cell membranes and improving one's cognitive function.

Keywords: Centella asiatica, phytosome, cell membrane, cognitive function


1. INTRODUCTION

The central nervous system functions as a signal sender in the body which consists mainly of neurons and glia, neurons function to send information throughout the body in the form of electrical signals along the axons. Oligodendrosit which is one type of glia in the central nervous system functions to produce myelin which wraps the axon as an insulator and if damaged will inhibit the process of electrical conduction in the axon so that the body's control functions will be disrupted.

There are several disorders of the central nervous system, such as in Parkinson's disease, Alzheimer's, and Traumatic Brain Injury (TBI). TBI is a central nervous system disorder caused by serious head trauma. In Indonesia, to be exact in DKI Jakarta, 53.4% of accident victims suffered severe injuries, especially on the head. In TBI there is a decrease in
membrane integrity characterized by damage to nerve membrane phospholipids. This continues with the inability of oligodendrocytes to carry out the myelination process on damaged nerve cell membranes. TBI also directly initiates oligodendrocyte apoptosis and axon damage which can reduce the synthesis of Neuregulin-1 (NRG-1) protein which plays a role in the formation of myelin. NRG-1 protein is induced by an Early Growth Response 2 (EGR2) transcription factor, also called Krox-20. Loss of nerve myelin if prolonged will allow a permanent decline in cognitive function.

Cytidine-5’diphosphocoline or CDP-choline is a chemical substance that is very identical to the phospholipid membrane of human cells. In Indonesia CDP-choline is known as citicoline which is the most commonly used neuroprotector drug. CDP-choline is known to repair and prevent further damage to nerve cell membranes due to trauma.

Traumatic Brain Injury (TBI) is a direct cause of mechanical disruption of brain tissue which is the main cause of death and disability in developed and developing countries. Every year, in the United States about 1.7 million people suffer from TBI (CDC, 2013). According to the 2007 Brain Trauma Foundation, TBI is most often caused by motor vehicle accidents, injuries when exercising, or falling. In Indonesia, to be exact in DKI Jakarta, 53.4% of accident victims suffered severe head injuries (Riyadina et al., 2009).

Recent evidence identifies the occurrence of axonal degeneration in the human brain after TBI. Axon damage causes a decrease in the synthesis of the protein Neuregulin-1 (NRG-1) so that no mielination process occurs. NRG-1 itself is modulated by a transcription factor named ERG2 or Krox-20. NRG-1 modulation in TBI will reduce functional impairment due to myelin damage.

CDP-choline is a chemical substance that is identical to the phospholipid membrane of human cells. In Indonesia, CDP-choline is known as citicoline as the most commonly used neuroprotector drug. CDP-choline is known to repair and prevent further damage to nerve cell membranes damaged by trauma (Bekar et al, 2007). On the other hand, Indonesia still uses CDP-choline as the main neuroprotector drug. Therefore, this paper specifically reviews the potential of the plant extracts for the recovery of nerve cell membranes and improving one’s cognitive function.

2. PRINCIPAL REVIEW
2.1. Phytosome
Phytosome is a technology developed from the manufacture of drugs and nutraceuticals to combine extracts from plants that are soluble in phytoconstituents into phospholipids to form complex lipid molecules. The advantages of phytosome include increasing therapeutic benefits by increasing the solubility of phytoconstituent compounds in fat (Sharma and Roy, 2010).

2.2. Gotu Kola
Gotu Kola (Centella asiatica sp.) is an herbal plant that thrives in almost all regions of Indonesia. This plant has good gas absorption ability as well as other types of forest plants (Ludang, 2019; Ludang et al., 2018). Taxonomy Gotu Kola is classified into divisions: Spermatophyta, subdivisions: Angiospremae, class: Dicotyledenae, subclass: Polypetalae, nation: Umbellales, tribe: Umbilliferae (Apiasceae), genus: Centella, and species: asiatica (Sari, 2011). In ethnomedicine, Gotu Kola is used as sedative, antiepileptic, wound healing, anti-inflammatory and antioxidant agents. Gotu Kola has the ability to revitalize the brain and nervous system, increase attention span and concentration and antiaging (Gohil, 2010).
Gotu Kola extract with phytochemical content of triterpenoid saponin glycosides, namely asiaticoside, asiatic acid, madecassoside and madecasic acid (Alfarra and Omar, 2013) has a neuroprotective effect, one of which is by improving nerve function through activation of the Krox-20 regulatory gene as a transcription factor from NRG-protein 1 (Alfiantya et al., 2014). However, the Gotu Kola phytochemical components tend to be polar, so that the pharmacokinetics of active extracts using phytosome technology (Sharma and Roy, 2010) is needed. Phytosome Gotu Kola extract increased the amount of NRG-1 and a higher thickness of myelin in TBI model mice. It can increase the solubility of the Gotu Kola active substance in fat, so the organic/water partition becomes high (Al-Rosyid and Mangkoedihardjo, 2019). This significantly increase therapeutic benefits, and increase the absorption of active compounds where the chemical bonds between phosphatidylcholine and phytoconstituents show significant stability both (Sharma and Roy, 2010).

2.3. Nervous System

The nervous system is the body's control center starting from controlling and responding to changes in the environment, managing the mind, and regulating all the vital processes of the body such as blood pressure and breathing. The human nervous system is divided into two, namely the Central Nervous System (CNS) and the Edge Nervous System (SST). The human CNS consists of the brain and spinal cord which are a group of neuron and glia cells. Neurons send information throughout the body in the form of electrical signals along axons and the release of neurotransmitters at synapses. Glia consists of various types of cells that function to maintain and protect neurons. One of the glia cells is oligodendrocyte which plays a role in producing myelin, a lipid-rich membrane that wraps axons and functions as an electrical insulator. Myelin reduces capacitance across the membrane and increases electrical resistance thereby increasing the speed of electrical conduction in axons (Darbas, 2004).

2.4. Traumatic Brain Injury

Traumatic Brain Injury (TBI) is a direct mechanical disorder of brain tissue due to external forces on the head and can mediate extensive neurodegeneration (Albert and Shiren, 2010). In head trauma, primary brain damage occurs at the initial impact of trauma, whereas secondary brain damage is the result of processes after the trauma occurs (Onose et al, 2011). The first stage of brain injury after TBI is characterized by direct tissue damage and impaired blood flow to the brain. Ischemia causes accumulation of lactic acid due to anaerobic glycolysis, increased membrane permeability, and edema formation. The second stage is characterized by cell membrane depolarization along with excessive release of glutamate and aspartate neurotransmitters, activation of N-methyl-D-aspartate, α-aminoo-3-hydroxy-5-methyl-4-isoxazolpropionate, and voltage-dependent Ca2+ and Na+ -channel. Influx Ca2+ and Na+ respectively trigger intracellular catabolism. Ca2+ activates lipid peroxidase, protease, and phospholipase which increase intracellular concentrations of free fatty acids and free radicals. In addition, activation of caspases (ICE-like proteins), translocases, and endonuclease initiate progressive structural changes in biological membranes and nucleosomal DNA resulting in DNA fragmentation and inhibition of DNA repair. Simultaneously, these mechanisms cause membrane degradation of blood vessel structures and cell necrosis or apoptosis in cells (Werner, 2013).

Molecularly, TBI will cause disturbance of the brain's metabolic process by damaging myoanptic acid which causes the phospholipid membrane of nerve cells to form and damage the myelin layer (Narayana et al., 2014). When the nerve phospholipid membrane is damaged, the oligodendrocytes cannot wrap the damaged axon membrane so that myelination disorders occur. The absence of myelin formation will reduce the relationship between nerve cells so
that it interferes with the ability of the brain to process information that manifests as cognitive impairment (Huang et al., 2009).

2.5. CDP-Choline

CDP-choline (cytidine-50-diphosphocholine) or generic name Citicoline is one of the most widely used therapies for TBI patients in Indonesia. CDP-choline is a compound with wide benefits in conditions associated with symptoms of neurological dysfunction (Qureshi, 2010). There are several mechanisms of CDP-choline as a neuroprotector including by preventing the activation of phospholipase A2, preventing loss of cardiolipin, increasing platelet activation factors, effective in fat peroxidation and phosphatidylcholine suppliers as raw material for biosynthesis of cell membrane phospholipids (Grieb, 2014; Menku, 2014).

2.6. Phospholipids

Lipids play a structural and functional role in the brain where the brain is the organ with the highest lipid concentration after adipose tissue. Phospholipids are components of the structure of cell membranes involved in the transduction of intraneurone signals. Phospholipids are also involved in membrane transport and neurotransmission in the brain (Tayebati, 2013; Krishnan, 2013).

2.7. Gen Krox-20

Krox-20 (EGR-2) is one of the transcription factors that participate in myelination. The myelin gene is induced by Krox-20 as a myelination regulator (Ghislain, 2006). EGR-2 plays an important role in peripheral nerve myelination, adipogenesis, and immune tolerance (Fang, 2011).

2.8. Protein Neuregulin-1 (NRG-1)

NRG-1 is a growth factor that plays an important role in nerve development, repair, and remielination. This protein is mainly expressed at a critical time point after nerve injury (Krishnan, 2013). The loss of NRG-1 causes impaired remielination of nerves that are damaged due to injury or trauma. NRG-1 plays a role in the repair of nerve function in the initial phase of nerve damage (Fricker et al., 2013).

2.9. Cognitive Function

Cognitive refers to the capacity to process information, apply knowledge, and change cognitive preferences are complex ideas that involve at least memory, attention, executive function, perception, language, and psychomotor functions (Nehlig, 2010). Cognitive can be defined as the process used by an organism to organize information. This includes obtaining information (perception), choosing (attention), representing (understanding), retaining information (memory), and using information to guide behavior (reasoning and coordinating motor output) (Bostrom, 2009).

3. CONCLUSION

Phytosome potential of Gotu Kola extract as a neuroprotector is characterized by increased Krox-20 activation, NRG-1 expression, repair of nerve cell membranes, and increased cognitive function. Furthermore, this will serve as a basis for further research development in the field of health.
REFERENCES


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