WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 1, 219-236. Review Article ISSN 2277– 7105

# ROLE OF LIPIDS IN PREVENTION OF MENTAL DISEASES

**Rekha Shah*, Hem Raj Vashist and Shivani Dogra**

Department of Pharmacy L.R Institute of Pharmacy, Jabli-kyar, Oachghat, Solan (H.P), India.

Article Received on
23 October 2020,

Revised on 13 Nov. 2020,
Accepted on 03 Dec. 2020

DOI: 10.20959/wjpr20211-19362

***Corresponding Author**
**Rekha Shah**
Department of Pharmacy
L.R Institute of Pharmacy,
Jabli-kyar, Oachghat, Solan
(H.P), India.

## ABSTRACT

Lipids are the naturally occurring compounds which include mainly fats, oils, waxes, and phospholipids. They are obtained from plants and animal's origin. Lipid metabolism plays a significant role in CNS because it originates in higher concentrations. Brain is a central organ of the human body which consist of highest lipids, after adipose tissue. The role of lipids in tissue damage and cell signaling is indicated by varied neurological disorders. The present review aims to give an overview regarding lipids and its imbalances with CNS disorders such as Parkinson's, Schizophrenia, epilepsy, Multiple sclerosis, Alzheimer's disease and CNS injury including traumatic brain injury, stroke, and spinal cord injury. Moreover, the viable mechanisms of altered level of lipids and their metabolites have additionally been discussed in detail.

**KEYWORDS:** Lipids, Parkinson's disease, lipid peroxidation, CNS injury, Schizophrenia, epilepsy, Multiple sclerosis, Alzheimer's disease, traumatic brain injury, stroke, and spinal cord injury.

## 1. INTRODUCTION

### 1.1 Lipids and the CNS

Lipids are defined as a large group of naturally occurring compounds such as fats, waxes, oils, sterols, phospholipids, and others. Lipids are substances that are acquired from plants and animal's origin. They are comprised of Fixed oils, fats, and waxes.

Lipids are obtained by extraction or expression methods.[1]

Fats and oils provide energy to the body. They serve as transport forms of metabolic fuels.

They have defensive functions in plants, bacteria, insects, and vegetables.

It serves as pigment (carotene), hormones (VitA & D), detergent, cofactors (Vitamin E, K), and signaling molecules (steroids).[2]

### 1.2 Classification

Lipids are broadly classified into the following types:

**Table 1: Classification of lipids.**

| Simple | Compound | Derived |
|---|---|---|
| 1.. Fats and oils | 1.. Phospholipids | 1.. Fatty acids |
| 2.. Waxes | 2.. Glycolipids | 2.. Alcohol (glycerol, sterol) |
| | 3.. Lipoproteins | |

### 1.2.1 Simple lipids

Simple lipids are esters of fatty acids with various types of an alcohol group. E.g. Fats, oils, and waxes.

Fats and oils are stored forms of energy. They are also known as unsaturated fats. Fixed oils are a long chain of fatty acids, alcohol, and glycerol. Waxes are the esters of fatty acid with an alcohol.

**Utilizations of the fixed oils and fats**

1. Utilized in soap manufacturing
2. In suppositories and tablet coating
3. Also in dietary enhancements
4. Utilized as emulsifying agents
5. Utilized in manufacture of paints, varnishes, and lubricants
6. Therapeutic uses (castor oil).

**Waxes**

Waxes are esters of a long chain alcohol and a fatty acid. Waxes are found in nature as coatings on leaves and stems.

**Table 2: The major types of waxes.**

| Type | Examples |
|---|---|
| 1. Natural Waxes | |
| 1.1 Animal Waxes | Beeswax, Lanolin, Tallow |
| 1.2 Vegetable Waxes | Carnauba, Candelilla, Soy |
| 1.3 Mineral Waxes | |
| 1.3.1 Fossil or Earth | Ceresin, Montan |

| | |
|---|---|
| 1.3.2 Petroleum | |
| 1.3.2.1 Paraffin | Slack, Scale Wax, Refined Paraffin |
| 1.3.2.2 Microcrystalline | |
| 1.3.2.3 Petrolatum | |
| 2. Synthetic Waxes | |
| 2.1 Ethylene Polymers | Polyethylene, polyol ether-esters |

**USES OF WAX**

1. Wax is used in pharmacy to prepare lip balm.
2. The technical uses of waxes, e.g. in shoe polishes and car waxes.
3. Waxes are also used in making soft ointments.

**1.2.2 Compound lipids**

Compound lipids are esters of fatty acids with a group of alcohol.

E.g. phospholipids, glycolipids, and lipoproteins.

Phospholipids contain phosphoric acid.

**1.2.3 Derived lipids**

These include fatty acids, steroids, other alcohols, etc.

Derived lipids are the substances derived from simple and compound lipids by hydrolysis.

Fatty acids are the simplest form of lipids. Fatty acids are also known as acyl group when it is a part of ester. Fatty acids are further divided into saturated and unsaturated fatty acids.[3]

**1.3 Role of Lipids in the Central Nervous System**

Lipid metabolism plays a significant role for CNS because lipid originates in higher concentration, second to adipose tissue. Lipids have been beneficial for the brain. Lipids also participate in the brain for the maintenance and regulation of its activities. However, if the concentration of lipids is altered in the brain, it leads to worsening of the condition.

Brain disorders, CNS traumas, stroke, multiple diseases are the most issues within the clinical field.[4] However, there is no cure for these CNS injuries and disorders.

The role of lipids in tissue damage and cell signaling is diagrammatic by the varied neurological disorders like

- Alzheimer's disease,
- Parkinson's disease,

- Multiple disorders,
- Schizophrenia,
- Epilepsy,
- CNS injury (Stroke, traumas, brain injury, and funiculus injury).

Lipids in the brain are concerned with several metabolic pathways. The most important role of lipids in the brain is proliferation, cell growth, and neuroprotection.[5] Some lipids show their action by binding with receptors like sphingomyelin, G-protein coupled receptors. These lipids are called "neurolipids".

### 1.3.1 Sources of lipids to CNS

Blood-brain barrier considerably inhibits the entry of harmful substances in the CNS. Therefore, all the lipids found in CNS should be synthesized at intervals CNS. E.g. fatty acids, cholesterol of these are helpful for neurological performance.

Peroxisomal fatty acids reaction is very important within the brain because the brain contains very-long-chain fatty acids and open-chain fatty acids.

## 2. Lipids in CNS disorders

**Table 3: Lipid systems affected by the CNS disorders and injuries.[6]**

| Disorder/ injury | Symptoms/pathologic features | CNS region(s) affected | Mechanism of damage | Possible Treatments |
|---|---|---|---|---|
| Alzheimer Disease | > Memory loss<br>> Difficulty in communicating<br>> Problems learning, thinking, reasoning<br>> Difficulty with familiar tasks<br>> Disorientation<br>> Amyloid plaques and tau protein aggregation | > Amygdala<br>> Hippo-campus<br>> Cerebral cortical areas controlling reasoning, learning, and language | > Altered cholesterol and lipid homeostasis<br>> APP cleavage in lipid rafts<br>> DHA levels ↓; upregulation of $PLA_2$, increased lipid peroxidation<br>$sPLA_2$-IIA expression increased | > Ganglio-side treatments prevent neuronal death.<br>> ApoE protects against oxidative injury by mediating Aβ<br>> Statins |

| Disorder/ injury | Symptoms/pathologic features | CNS region(s) affected | Mechanism of damage | Possible Treatments |
|---|---|---|---|---|
| Parkinson's Diseases | > Movement disorder<br>> Resting tremors<br>> Muscle rigidity<br>> Bradykinesia (slow movemets)<br>> Impaired posture, balance, coordination<br>> Lewy bodies/α-synuclein aggregate | | > Although a direct role of $PLA_2$ in PD is not yet clearly demonstrated, $cPLA_2$ knock out mice showed protection against MPTP toxicity.<br>> PUFAs promote α - synuclein aggregation | > $PLA_2$ inhibition Ganglioside treatments Quinacrine |
| Multiple Sclerosis-Experimental Autoimmune Encephalomyelitis (MS-EAE) | > Unpredictable and varies from person to person<br>> Loss of balance<br>> Loss of muscle coordination, resulting in tremors, bladder problems and slurred speech.<br>> Problems with memory, attention, cognitive functions. | Demyelination of axons | > Lipid peroxidation products from ROS.<br>> $cPLA_2$ is highly expressed in EAE.<br>>sPLA2 levels increased prior to onset of symptoms.<br>> T cells and auto-antibodies to Lipids<br>> DHA levels ↓ | > Antioxidants<br>>sPLA2 inhibition by CHEC-9 blocks inflammation.<br>> Ganglioside treatments prevent neuronal death. |
| Schizophrenia | > Disturbances in thinking, emotional reactions, and social behaviour | > Dorsalateral prefrontal cortex | > Altered lipid metabolism may be responsible for defects in neurological development | > Antipsychotic drugs<br>> Eicosapentaenoic acid supplementation |
| Epilepsy | > Wide range of severity | > Focal cortical area, later transferred | > DHA levels ↓ | Ketogenic diet Phenytoin |
| | > Violent convulsions<br>> Loss of consciousness<br>> Minimal or no | to the Thalamus | | > Second generation antiepileptic drugs |

| Disorder/ injury | Symptoms/pathologic features | CNS region(s) affected | Mechanism of damage | Possible Treatments |
|---|---|---|---|---|
| | movements | | | |
| Stroke | > Sudden weakness on one side of the body, loss of balance and coordination, trouble with cognition | > Cerebral cortical Areas<br>> Striatum | > Activation of Phospholipases ($A_2$, C, D), increased $sPLA_2$<br>> $cPLA_2$ knock out mice showed protection [4 and references Cited therein]<br>> DHA levels ↓ | > CDP-choline attenuated $sPLA_2$<br>> Neuroprotectin D1 reduces infarct in MCAO model<br>> $sPLA_2$ inhibitors |
| Traumatic Brain Injury | | > Loss of $CA_3$ hippocampal neurons | > Aβ deposition, tau pathology | > Corticosteroids<br>> apoE mimetic peptide showed benefit in experimental TBI |
| Spinal Cord Injury | > Weakness and sensory loss; paralysis | | > Activation of $PLA_2$, COX/LOX pathways. Corticosteroids inhibit These activations | > High-dose methylprednisolone in clinical use ; DHA treatment is beneficial |

### 2.1 Parkinson's disease

Parkinson's disease may be a progressive nervous system disorder that affects movement, usually together with tremors. The disorder also causes stiffness or reduces speed of movement. There is no etiology of Parkinson's disease (PD). The most pathological characteristics of PD are necrobiosis within the brain's basal ganglia and also the presence of Lewy bodies in several of the remaining neurons.[7] This loss of neurons during the death of astrocytes (star-shaped glial interstitial cells) and a major increase within the range of neuroglia (another sort of glial cell) within the neural structure. Shockingly, a few investigations have additionally detailed that there is no affiliation between advancement of PD and cholesterol levels. Additionally, low degrees of complete cholesterol (TC), HDL-C and LDL-C have been seen in the PD patients.[8] Reaction stress and lipid peroxidation plays a vital role in pathogenesis of PD.

### 2.1.1 Treatment of PD

No therapy to delay the loss of dopamine neurons in PD has been demonstrated. The dopamine prodrug levodopa continues to be the gold standard for treating PD. Long-term levodopa treatment does, however, contribute to dyskinesia progressing. However, pallidotomy and thalamotomy may be performed in selected patients, deep brain stimulation is that the operation for PD patients.

Some medicines such as Carbidopa and Levodopa are utilized in the treatment of Parkinson's disease. Levodopa is the most effective medication for the treatment. It is continually given within the combination with carbidopa to stop decarboxylation. It is used as a symptomatic treatment for early PD. Monoamine neurotransmitter agonists stimulate monoamine neurotransmitter receptors directly and also the second most potent category of medication.[8] Amantadine's mechanism of action remains unknown; however, in addition to acting as an antagonist to the NMDA receptor, it has been reported to have anticholinergic properties to enhance dopamine release and prevent its reuptake. However, these procedures remain based on symptomatic relief while reducing the adverse effects.

### 2.1.2 PD, oxidative stress & lipid peroxidation

In Parkinson's disease (PD), the metabolism of monoamine neurotransmitters by the monoamine-oxidase-B may lead to excessive reactive oxygen species formation. A role for oxidative stress in PD was denoted by increase in 8-hydroxy-2`-deoxyguanosine, a hydroxyl radical-damaged guanine nucleotide commonly used to evaluate oxidative DNA damage. Further, there are several markers of lipid peroxidation that were found to be enlarged in PD brain regions.[9]

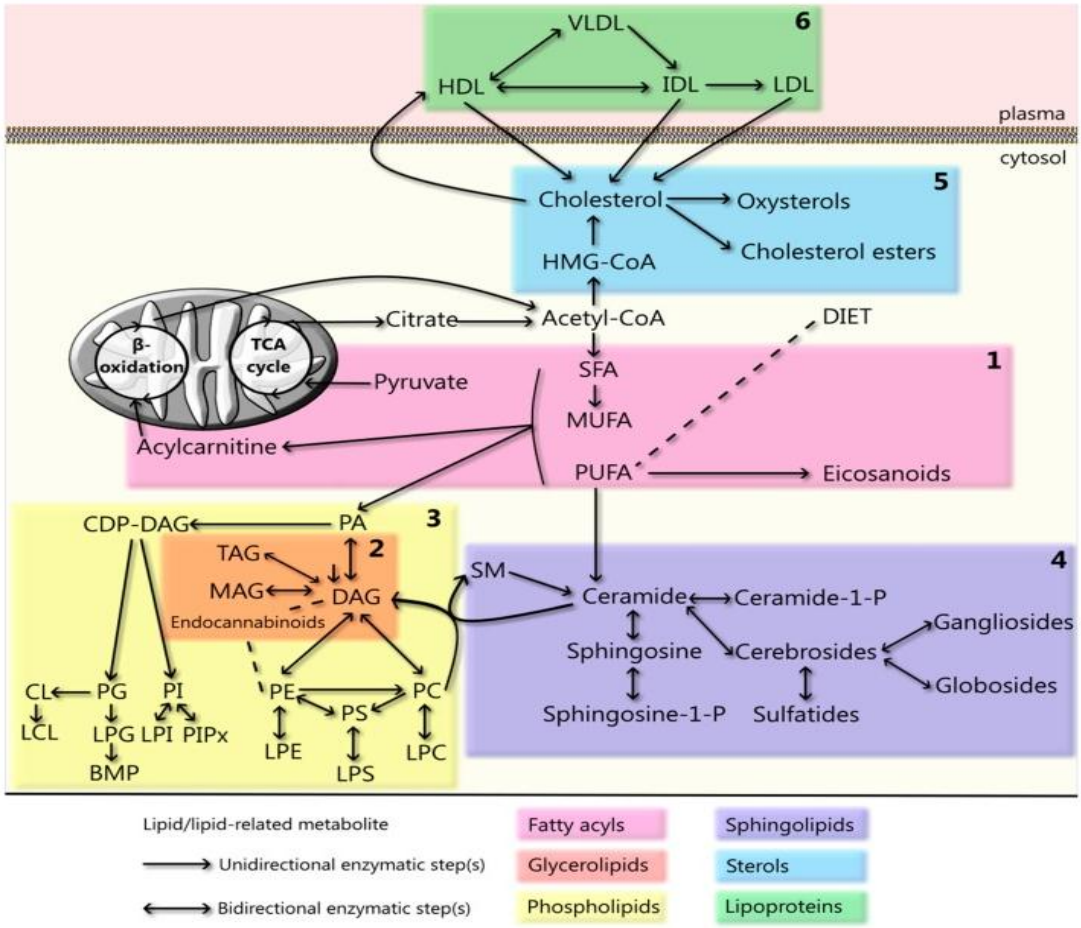


**Fig 1: Lipid metabolism in Parkinson's disease.[10]**

### 2.2 Schizophrenia & epilepsy

Schizophrenia is a disorder that affects a person's ability to assume or behave. It is a heavy disturbance and will result in hallucinations, very disordered thinking, and behavior. It impacts thinking, emotions, speech, and alterations areas of life. Schizophrenia may be a fairly uncommon condition, moving around 0.25% to 0.64% of individuals within the United States, consistent with the National Institute of Mental Health (NIMH). Schizophrenia disorder may be a lifelong condition however effective treatment can help to overcome the situation.[11]

Latest theories on the Schizophrenia have focused on abnormalities in lipid metabolism, in particular increased activity of PLA2 enzymes, and reduced activity of the system which includes PUFAs into phospholipids.[11] These abnormalities lead to changes in the structure of the membrane and so the function of membrane-bound proteins and also the behavior of neurotransmitter systems. Therefore, lipid metabolism has a vital role in neuronal

growth.[11,12] It's been found that schizophrenia is associated with lipid transport proteins and membrane phospholipid composition.

From a restorative point of view, various reports demonstrate that in any event a bit of schizophrenic patients have decreased degrees of PUFAs, especially ArAc and DHA, in red cell phospholipids, with low levels especially connected with negative indications. ArAc, DHA and eicosapentaenoic corrosive (EPA) are significant for monoaminergic neurotransmission, mental health, and synaptic working.[12] This recommends supplementation with basic unsaturated fats could ease indications of schizophrenia. In starter examines, in any case, DHA basically had no impact and ArAc seemed to compound indications in some schizophrenia patients.[11]

Latest findings indicate the function of oxidative stress-induced abnormalities and changes of membrane phospholipids and fatty acids in etiopathogenic pathways in schizophrenia where the oxidative metabolites derived from membrane lipids, including prostaglandins and isoprostanes, had been identified.[13] In addition, schizophrenia may be associated with altered metabolism of polyunsaturated fatty acids (PUFA), particularly arachidonic acid and cell membrane phospholipids.[11,13]

**Epilepsy**

Epilepsy is a neurological disorder that causes unverified, repeated seizures. A seizure may be an explosive rush of electrical activity within the brain. Seizures can also lead to the death of brain cells.[14] Epilepsy is also called a seizure disorder. Epilepsy is treated with a medicine called ant-epileptic drugs. Phenytoin is the widely used anti-epileptic medicine.[15] The essential site of action appears to be the motor cortex, where the spread of seizure activity is inhibited by advancing sodium efflux from neurons.

The ketogenic diet is an efficient non-pharmacological symptomatic treatment for epilepsy.[16] The ketogenic diet is a very high fat, low carbohydrate, controlled macromolecule diet. This diet is used since 1920s for the treatment of epilepsy.[17] Despite its use for several years, there is still a tidy discussion over how the ketogenic diet works.

Elevated cholesterol is involved in several initiating disorders of both neurological and neurodegenerative type. Cholesterol is degraded by an enzyme named as cholesterol 24-Hydroxylase, encoded by the gene CYP46A1. Apparently, by the inhibition of this catabolic

enzyme, cholesterol level in the neurons of hippocampus increases. In turn this increased cholesterol outcomes in the neuronal cell death and deviant hippocampus synchronies.[18]

### 2.3 Alzheimer's disease

Alzheimer's disease (AD) is a progressive disease that destroys memory and alternative mental functions. Neuron connections and also the cells themselves degenerate and die, eventually destroying memory and alternative mental functions. Alzheimer's disease is broadly divided into early-onset AD (occurring in persons under age 65 years, 5-10% of AD) and late-onset (90-95% of AD).

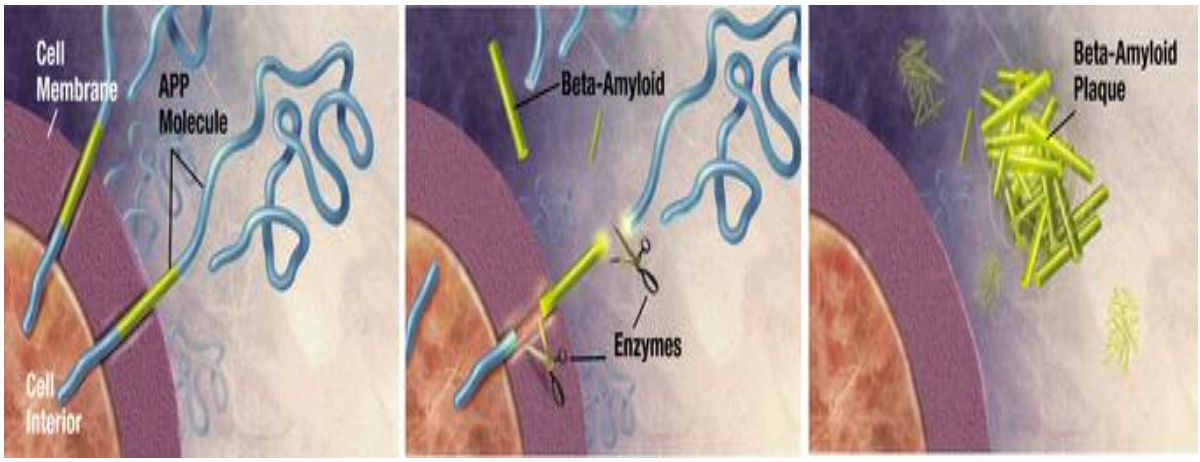


**Fig. 2: Amyloid Plaque Formation: Enzymes act on the APP (Amyloid precursor protein) and cut it into fragments of protein, one of which is called beta-amyloid and it's crucial in the formation of senile plaques in AD.[19]**

One of the hallmarks of AD is the overproduction of a 4-kDa peptide, amyloid peptide resulting in the formation of plaques. The other hallmark of AD is the formation of neurofibrillary tangles because of the hyperphosphorylation of tau proteins. Whereas the etiology of AD is unknown, notable risk factors for the disease include increasing age, positive family history. Theories relating to AD specialize in the abnormalities of the brain involving the nervous system. There is evidence that cholesterol is of importance in the development and progression of the disease.[20] Apolipoprotein (Apo) E is one of the major Apos in plasma and the principal cholesterol carrier protein in the brain.

#### 2.3.1 AD, oxidative stress & lipid peroxidation

A number of studies demonstrating increased amount of lipid peroxidation in AD provide mounting evidence supporting a role for oxidative damage in this disorder. In recent studies,

increased levels of hydroxynonenal (HNE) and acrolein,[21] in the brain tissue from patients affected by early AD, shows that lipid peroxidation occurs early in the pathogenesis of AD.[21] Acrolein, the strongest electrophile among all α,β-unsaturated aldehydes, reacts with DNA bases such as guanine, adenine, cytosine, and thymidine to form cyclic adducts, the main cyclic adducts is acrolein-deoxyguanosine. Increased levels of acrolein-deoxyguanosine adducts were denoted in brain tissue from AD patients. Reactive oxygen species (ROS) may also play a role in amyloid deposition in AD as oxidizing conditions cause protein cross-linking and aggregation of Aβ peptides; Aβ aggregation has been shown to induce ROS accumulation, which may result in cyclical or self-propagating oxidative damage.[21] This indicates that oxidative stress plays an important pathological function in the development of disease.

### 2.4 Multiple sclerosis

Multiple sclerosis (MS) may be a potentially disabling disease of the brain and spinal cord. In MS, the immune system attacks the protective sheath that covers the nerve fibers and causes communication problems between the brain and the body. Eventually, this disease can cause permanent damage or deterioration of the nerves.

It is predominantly a T-lymphocyte-mediated disorder and cytokines have a key role in the pathogenesis of the disease. Multiple sclerosis is the only neurological disorder where therapeutic manipulation of the cytokine system influences the disease. Thiobarbituric acid substances and F2-isoprostane levels were shown in MS patients, and HNE was indicative that lipid peroxidation also occurs in multiple sclerosis. The metabolism of lipids in the body may have direct and indirect effects on multiple sclerosis disability and disease progression due to the fact they are essential for regulating inflammatory responses and for re-myelination and repair in the CNS and disruption of lipid homeostasis can affect myelin integrity and modulate neurodegeneration.

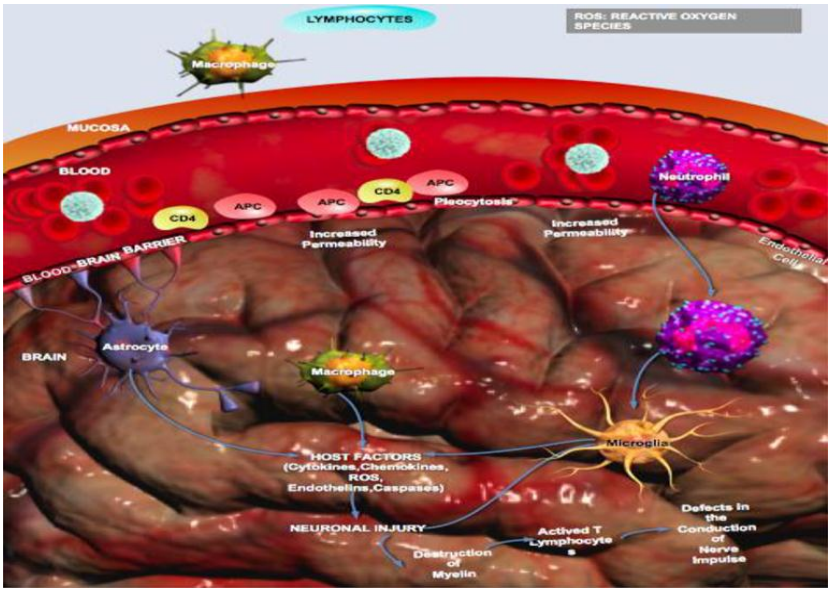


**Fig. 3: Immune-mediated destruction of myelin components in multiple sclerosis.**[22]

In Marrie and colleagues study, the presence of hypercholesterolemia at any time throughout the disorder course was associated with 35% increased risk of early gait disability, 33% increased risk of unilateral walking assistance and 24% increased risk of bilateral walking assistance. From these it is clear studies which affect cholesterol levels increase in impairment levels. On the whole, evidence from the studies indicates a negative effect of high TC, LDL and triglycerides on acute inflammatory activity, disease course in patients with MS and a useful impact of higher HDL levels on MS.[23]

## 3. Lipids in CNS injury

### 3.1 Stroke

A stroke occurs when the blood supply to part of the brain is interrupted or severely reduced, depriving brain tissue of oxygen and food. Stroke is the abrupt onset of a neurological deficit. Stroke is also known as Focal cerebral ischemia.

For the treatment of ischemic stroke, tissue plasminogen activator (tPA) is the only drug approved by the US FDA.

The primary event in ischemia stroke is energy failure, resulting in excessive release of the neurotransmitters (dopamine & glutamate).

In many epidemiological units, there is a direct relationship between cholesterol levels and ischemic stroke. The relationship of lipids to ischemic stroke varies by stroke subtypes.

Eventually, there is an increased risk of intracerebral haemorrhage and small vessel disease at low levels of cholesterol.

Excessive stimulation of glutamate receptors results in elevated intracellular Ca2+ and activation of phospholipases A2, C, and D. Stimulation of these phospholipases causes hydrolysis of membrane phospholipids and release of second messengers. The nature of the inflammatory response after stroke suggests that cytokines affect phospholipid metabolism and free radicals that enhance brain injury. Several studies have reported the impaired fatty acids metabolism with the increased risk of disease. Namely, low level of linoleic acid in platelets, erythrocytes, adipose tissue and blood are related with the increased risk of Ischemia Stroke and total stroke. In a case study, it was found that FAs alteration is involved in the progression of various subtypes of stroke. Like low level of linoleic acid can accelerate the stroke whereas, high levels of serum SFAs and ω-3 PUFAs have been found to be related with haemorrhagic stroke.[24]

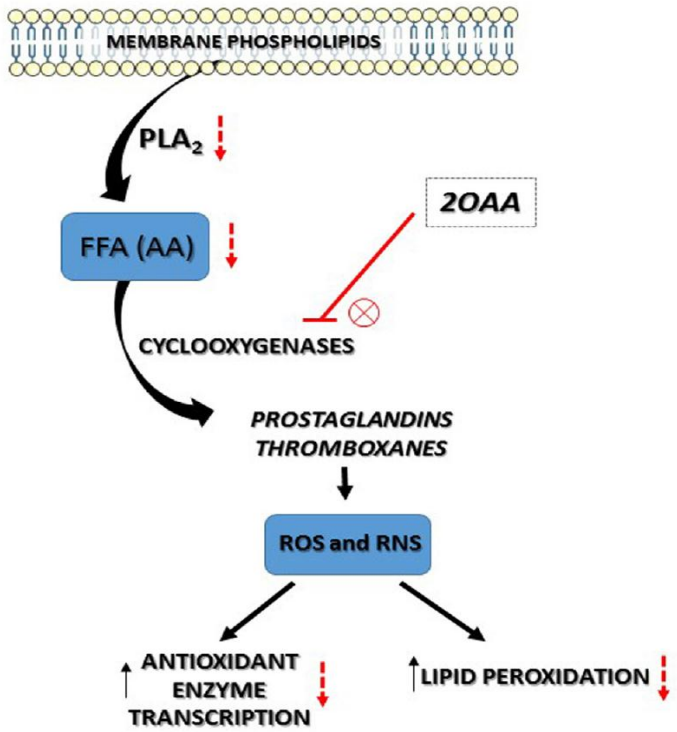


**Fig. 4: Lipid peroxidation in stroke.**[25]

### 3.1.1 Stroke, ROS & lipid peroxidation

As yet, it has been believed that the oxidative metabolism of ArAc through COX causes prostaglandins and ROS. Few studies have mentioned that COX-2 generates tyrosyl radicals on the protein and carbon-centred radicals on the substrate ArAc, but does not produce ROS.

It has appeared that ROS production was raised in a stroke model but that COX-2 inhibition did not reduce ROS production. Although, ROS generation was not reduced in COX-2 deficient mice. These studies revealed that NADPH oxidase was an important source of ROS in the stroke model.[4] The role of ROS is in stimulating various signaling pathways including matrix metaloproteinases, NF-kB, and stroke injury has been reviewed.[26]

The time course of variations in lipid metabolism and formation of lipid metabolites and lipid peroxidation products after transient cerebral ischemia are conferred.[27]

### 3.2 Traumatic brain injury

Traumatic brain injury (TBI) is the leading cause of death and disability in children and adults between the ages of 1 to 44. TBI is a non-degenerative, non-congenital insult in the brain from an external mechanical force, with an associated altered state of consciousness. TBI may be divided into primary and secondary injuries.

The pathways of secondary injury that take place after the primary trauma present targets for therapeutic interventions are correlative to stroke.[28] Corticosteroids have been determined as therapies to reduce the secondary injuries following Traumatic Brain Injury (TBI). Corticosteroids inhibit the PLA2/COX/LOX pathways, thus limiting ArAc release and metabolism, down-regulating pro-inflammatory cytokines and increasing the inflammatory response.

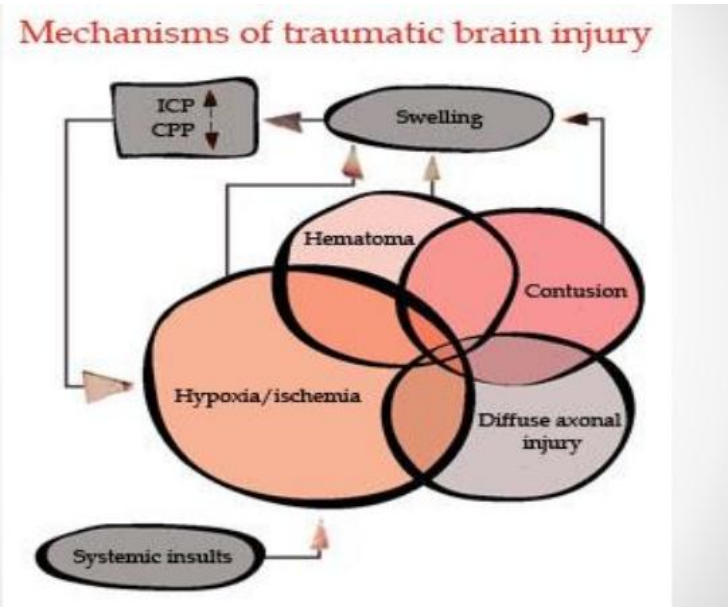


**Fig. 5: Mechanisms of traumatic brain injury.**[29]

### 3.3 Spinal cord injury

Spinal cord injury (SCI) is damage to any part of the spinal cord or nerves at the end of the spinal canal- often causes permanent changes in strength, sensation and other body functions below the site of the injury. SCI, as with acute stroke, is a dynamic process. SCI is the result of an initial physical trauma followed by a secondary degenerative process. The majority of SCI do not involve physical transaction of the spinal cord; instead, the cord is injured as a result of contusive, compressive, or stretch injury. The primary event after SCI is depolarization and opening of voltage depending ion channels, and consequent massive release of neurotransmitters, like glutamate. This results in to accumulation of intracellular calcium, initiating a variety of damaging events: mitochondrial dysfunction, activation of nitric oxide synthase (NOS) and $PLA_2$.[30]

The glucocorticoid steroids dexamethasone and methylprednisolone are used in the clinical treatment of SCI. The preliminary rationale was that, since these compounds reduced brain edema in brain tumor patients, they would also reduce edema in SCI. It is believed that inhibition of lipid peroxidation is the principle neuroprotective mechanism of high dose methylprednisolone and that glucocorticoid receptor-mediated anti-inflammatory effects have only a minor part.[30] The levels of apolipoprotein-A1 were found to be decreased and the concentrations of apolipoprotein-B increased in people with SCI.

## 4. CONCLUSION

The group of lipids plays an important role in the cell and tissue. The concept of the review has been introduced to describe the role of lipids in the brain and CNS disorders. Several types of researches recommend that many lipids are involved in the maintenance of the regulation of inflammation and pain, energy metabolism, and development of the brain in the nervous system. More profound information on the nature of lipid signaling will promote our comprehensive of the role of lipid metabolism in different CNS disorders, opening new doors for improvement and treatments for neurological diseases. The connection behind the altered lipid metabolism and brain functions depends on the beginning of various brain disorders such as Schizophrenia, AD, PD, epilepsy, multiple sclerosis as well as brain injuries such as stroke, trauma, and spinal cord injury. Besides, in this review, the relationship between lipid metabolism and neurological diseases has been discussed in detail.

**Ethical Approval**

It is not applicable.

**CONFLICT OF INTEREST**

The authors confirm that this article has no conflict of interest.

**ACKNOWLEDGEMENT**

I am very thankful to my teacher Dr. Hem Raj Vashist for his constant support and guidance.

**REFERENCES**

1. Kokate C.K., A. P. Purohit, Gokhale S.B., Pharmacognosy 13th edition, Nirali Prakashan, Page. 10.1-10.84. Jain P, Surana SJ (2015) A review of Indian medicinal plants with hypolipidemic activity and their medicinal importance. World Journal of Pharmacy and Pharmaceutical Sciences, 2002; 4(3): 1477-1493.
2. Lipid Library: Lipid Chemistry, Biology, Technology & Analysis http://lipidlibrary.aocs.org/.
3. Fahy E, Subramaniam S, Brown HA et al.: A comprehensive classification system for lipids. J. Lipid Res., 2005; 46(5): 839–862.
4. Adibhatla RM, Hatcher JF, Dempsey RJ: Lipids and lipidomics in brain injury and diseases. AAPS J., 2006; 8(2): E314–E321.
5. Wenk MR: The emerging field of lipidomics. Nat. Rev. Drug Discover, 2005; 4(7): 594–610. Excellent comprehensive review on various aspects of lipidomics and bioinformatics. 2A comprehensive classification system for lipids. J. Lipid Res., 2005; 46(5): 839–862.
6. Adibhatla RM, Hatcher JF, Dempsey RJ. Lipids and lipidomics in brain injury and diseases. AAPS J., 2006; 8(2): E314–E321.
7. Hauser RA, Zesiewicz TA: Advances in the pharmacologic management of early Parkinson disease. Neurologist, 2007; 13(3): 126–132.
8. Samadi P, Grégoire L, Rouillard C et al.: Docosahexaenoic acid reduces levodopainduced dyskinesia in 1-methyl-4-phenyl1, 2, 3, 6-tetrahydropyridine monkeys. Ann. Neurol, 2006; 59(2): 282–288.
9. Hauser RA, Zesiewicz TA: Advances in the pharmacologic management of early Parkinson disease. Neurologist, 2007; 13(3): 126–132.
10. Xicoy H, Wieringa B, Martens GJ: Lipids in Parkinson disease. Cells, 2019; 8(1): 27.
11. Horrobin D: The lipid hypothesis of schizophrenia. In: Brain Lipids and Disorders in

Biological Psychiatry. Skinner ER (Ed.), Elsevier Science, Amsterdam, the Netherlands, 2002; 39–52.

12. Berger GE, Smesny S, Amminger GP: Bioactive lipids in schizophrenia. Int. Rev. Psychiatry, 2006; 18(2): 85–98.
13. Fendri C, Mechri A, Khiari G, Othman A, Gaha L: Oxidative stress improvement n schizophrenia pathophysiology. Encephale, 2006; 32: 244-252.
14. Bialer M, Johannessen SI, Kupferberg HJ, Levy RH, Perucca E, Tomson T: Progress report on new antiepileptic drugs: a summary of the Eighth Eilat Conference (EILAT VIII). Epilepsy Research, 2007; 73(1): 1–52 Review of the new generation anti-epileptic drugs.
15. Klotz U: The role of pharmacogenetics in the metabolism of antiepileptic drugs: pharmacokinetic and therapeutic implications. Clin. Pharmacokinetic, 2007; 46(4): 271–279.
16. Papandreou D, Pavlou E, Kalimeri E, Mavromichalis I: The ketogenic diet in children with epilepsy. Br. J. Nutr, 2006; 95(1): 5–13.
17. Bough KJ, Rho JM: Anticonvulsant mechanisms of the ketogenic diet. Epilepsy, 2007; 48(1): 43–58.
18. Gasior M, Rogawski MA, Hartman AL: Neuroprotective and disease-modifying effects of the ketogenic diet. Behave. Pharmacol, 2006; 17(5–6): 431–439.
19. https://upload.wikimedia.org/wikipedia/commons/f/fb/Amyloid-plaque_formation-big.jpg
20. Mandavilli A: The amyloid code. Nat. Med, 2006; 12(7): 747–751. Provocative commentary on the current amyloid theories in Alzheimer's disease (AD).
21. Williams TI, Lynn BC, Markesbery WR, & Lovell MA: Increased levels of 4-hydroxynonenal and acrolein, neurotoxic markers of lipid peroxidation, in the brain in mild cognitive impairment and early Alzheimer's disease. Neurobiol. Aging, 2006; 27(8): 1094–1099.
22. Ramirez-Ramirez V, Macias-Islas MA, Ortiz GG, Pacheco-Moises F, Torres-Sanchez ED, et al. Efficacy of fish oil on serum of TNF-α, IL-1 β, and IL-6 oxidative stress markers in multiple sclerosis treated with interferon beta-1b. Oxid Med Cell Longev, 2013; 2013: 709493.
23. Marrie RA, Rudick R, Horwitz R et al. Vascular comorbidity is associated with more rapid disability progression in multiple sclerosis. Neurology, 2010; 74: 1041–1047.
24. Adibhatla RM, Dempsey RJ, Hatcher JF: Integration of cytokine biology and lipid

metabolism in stroke. Front Neurosurg. Res. (under the aegis of Front Biosci). (In Press), 2007.

25. Ugidos IF, Pérez-Rodríguez D, Fernández-López A. A role for lipids as agents to alleviate stroke damage: the neuroprotective effect of 2-hydroxy arachidonic acid. Neural Regen Res [cited 2020 Jul 18], 2017; 12: 1273-5.
26. Adibhatla RM, Hatcher JF: Phospholipase A2, reactive oxygen species, and lipid peroxidation in cerebral ischemia. Free Radic. Biol. Med, 2006; 40(3): 376–387.
27. Liu KJ, Rosenberg GA: Matrix metaloproteinases and free radicals in cerebral ischemia. Free Radic. Biol. Med, 2005; 39(1): 71–80.
28. Rigg JL, Zafonte RD: Corticosteroids in TBI: is the story closed? J. Head Trauma Rehab, 2006; 21(3): 285–288.
29. https://www.google.com/imgres?imgurl=https%3A%2F%2Fimage.slidesharecdn.com%2Ftbi-140824231703-phpapp02%2F95%2Ftraumatic-brain-injury-8-.
30. Hall ED, Springer JE: Neuroprotection and acute spinal cord injury: a reappraisal. NeuroRx, 2004; 1(1): 80–100.