IJBPAS, July, 2024, 13(7): 3190-3202

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

A COMPREHENSIVE REVIEW OF THE MEDICINAL AND THERAPEUTIC POTENTIAL OF *CURCUMA CAESIA* ROXB

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Received 15th March 2023; Revised 8th July 2023; Accepted 5th Oct. 2023; Available online 1st July 2024

https://doi.org/10.31032/IJBPAS/2024/13.7.8132

ABSTRACT

Black turmeric, an herb long known for its therapeutic benefits, has piqued the curiosity of medical/scientific researchers. Scientifically known as *Curcuma caesia Roxb*, is a rare medicinal plant found in the country's mountainous regions. It is a plant having the greatest curcumin concentration of any curcuma species, a chemical compound with several medicinal effects. This review paper focuses on the medicinal and therapeutic uses of *Curcuma caesia Roxb*. Various research and studies have found that the herb possesses biological properties like antibacterial, muscle relaxant, anti-asthmatic, anti-cancer properties, and many others. Curcumin which is present in the highest amount in this species acts as an anti-inflammatory and antioxidant in Alzheimer's. Rhizomes have historically been used to cure a variety of diseases and metabolic abnormalities such as asthma, tumors, and leukoderma. The review also covers the mechanism of action of *Curcuma caesia Roxb* on various diseases such as Amnesia, Alzheimer's, Anxiety, Depression, and Cancer. Therefore, the pattern and treatments of the crucial disease can be studied which may be further utilized for practical needs.

Keywords: *Curcuma caesia Roxb*, curcumin, rhizomes, biological properties, therapeutic uses

INTRODUCTION

The Zingiberaceae family contains the plant *Curcuma caesia Roxb*, Kali Haldi. It is mostly found in the states of West Bengal, Madhya Pradesh, Orissa, Chhattisgarh, Uttar Pradesh, and Gujarat. In damp deciduous woodland regions, it thrives well **[1]**. The plant's Rhizomes are used to make cosmetics and for treating bruises and sprains **[2]**. The different species of Curcuma have different benefits.

Rhizome's interior portion is blue-black in colour and gives off a distinctive sweet scent. These roots are used by "turkomans" (Turks) as a rubefacient to rub the body after a Turkish bath. The plant is highly considered as lucky and is frequently utilized in India for a variety of magical treatments **[3]**. The herb's rhizomes are often used to cure pneumonia, coughing, and colds in children, as well as fever and asthma in adults. Additionally, it is consumed in n piles, asthma, tumors, leukoderma, bronchitis and tuberculous glands of the neck, spleen enlargement, and allergic eruptions. *Curcuma caesia* rhizome has a flavour that is spicy, bitter, and harsh, and has a good aroma and it is moderately laxative in nature. It has antifungal and antibacterial effects and is consumed as a heart and brain tonic.

The Indian Agricultural Department has designated black turmeric as an endangered species as of 2016. In Odisha, on the Bay of Bengal's central eastern coast, efforts are being done to safeguard and conserve Black turmeric. The benefits offered by black turmeric are comparable to those of orange turmeric, although the darker cultivar has the highest curcumin content of any Curcuma species **[4]**.

According to reports, *C. caesia* rhizomes contain a variety of bioactive compounds utilized in the pharmaceutical industry, including flavonoids, alkaloids, sesquiterpene, and phenol. Herbal remedies are becoming highly popular nowadays since they are safer than medications based on chemicals **[5]**. To create herbal medicines, secondary metabolites are increasingly being extracted from plants. Supercritical fluid extraction (SFE) is a potent approach for separating natural chemicals from plants because it uses fluids in their supercritical states for the extraction of solid materials **[6]**. Several studies have been conducted in recent years on SFE's claimed industrial uses, which have advantages over traditional methods in the food, chemical, pharmaceutical, and oil sectors **[7]**. Due to the SFE method's use of less toxic solvent, extraction of heat-labile metabolites, and contamination-free result, it offers an advantage over conventional techniques of extraction **[8]**.

According to behavioural research using the Elevated Plus Maze and Morris Water

Maze, the Rhizome fractions and essential oil of *Curcuma caesia* may have considerable good therapeutic benefits on anxiety, and depression, and may even improve memory **[9]**. According to brain histology research, suppression of acetylcholinesterase enzymes and regeneration of neural cells can further raise acetylcholine levels in the brain's cholinergic cells. Its precise mechanism of neuroprotective activity would be substantiated by the discovery of the active molecule causing these activities and future research on a molecular level **[10]**.

Table 1: Diseases cured by various species of Curcumin

SPECIES	DISEASES CURED
***Curcuma longa* Linn.**	**It is laxative, anthelmintic, and vulnerary, used in blood disorders, leukoderma, scabies, smallpox, and sprains**
***Curcuma amada* Roxb.**	**Bronchitis, asthma, sprains, skin disease, and inflammation due to injuries**
***Curcuma aromatica* Salisb**	**Wound healing, anti-inflammatory, antiproliferative, and blood purifier activity**
***Curcuma zedoaria* Christm.**	**Antimutagenic, anticarcinogenic, as well as anti-inflammatory**
Curcuma angustifolia	**Aphrodisiac and treatment of leprosy, asthma, anemia, leukoderma**

Although a faulty MisMatch Repair (MMR) has been linked to solid tumors, its significance in hematological malignancies has received less attention, and current research shows that it has very little impact. Nevertheless, there are several paths that mismatch repair proteins can go through in hematologic malignancies, and these pathways could directly or indirectly facilitate the advancement of the illness **[11]**. However, by employing several Curcuma derivatives (*Curcuma longa L.* and *Curcuma caesia Roxb*.), that target proteins through computational analysis can be implicated in the rewiring of numerous signalling cascades. This process can change the expression in cancer, which in turn, drastically alters MMR protein function. These macromolecules were examined by some researchers to see how well they affected certain targets (in malignancies associated with the blood) and aberrations of these targets, which showed a negative effect on mismatch repair machinery. These findings suggest the possibility of plant-derived biomolecules with anticancer capabilities against cancers caused by aberrant MMR pathways **[12]**. Because of the presence of flavonoids and phenols in rhizome extract, research on *C. caesia* has so far proven its shielding effect in case of toxicity and cancer as well as its antioxidant. The phenolics are a class of compounds that have hydroxyl groups connected to their benzene structure, which allows them to function as free radical scavengers **[13]**.

Mechanism Of Neuroprotective Potential of *Curcuma caesia* against Amnesia and Alzheimer's Diseases

Amnesia is a memory deficiency turned on by brain disease or injury **[14]** but it can also

be momentarily brought on by the use of several sedatives and hypnotic medications. Based on the amount of the injury, the memory may be completely or partially lost **[15]**. Anterograde amnesia and retrograde amnesia are the two basic categories of amnesia. The impairment of memory that results from amnesia disturbs daily activities. Alzheimer's disease (AD) is a neurological condition that typically develops gradually and gets worse over time **[16]**. It is the root cause of 60–70% of dementia cases **[17]**. The most prevalent initial sign is trouble recalling recent events **[18]**. Language difficulties, disorientation (including a tendency to get lost easily), mood swings, a lack of desire, self-neglect, and behavioural problems are indicators of advanced Alzheimer's disease **[16]**. The main reasons for forgetfulness include neurological, genetic, chemical, environmental, functional, oxidative stress, family history, A-induced neurotoxicity, tau pathology, mitochondrial dysfunction, and metal dyshomeostasis of Alzheimer's disease **[19]**.

The method by which Alzheimer's Disease destroys nerve cells is thought to entail several characteristics, including metal toxicity, beta-amyloid plaque development, oxidative damage, and inflammation **[20]**. There are several mechanisms by which curcumin enables to treat the AD such as

- Action of Curcumin on Glial cells
- Action of Curcumin as an anti-oxidant in Alzheimer's
- Reduction in Beta-Amyloid plaques
- Action of Curcumin as an anti-inflammatory in Alzheimer's
- Metal Chelation

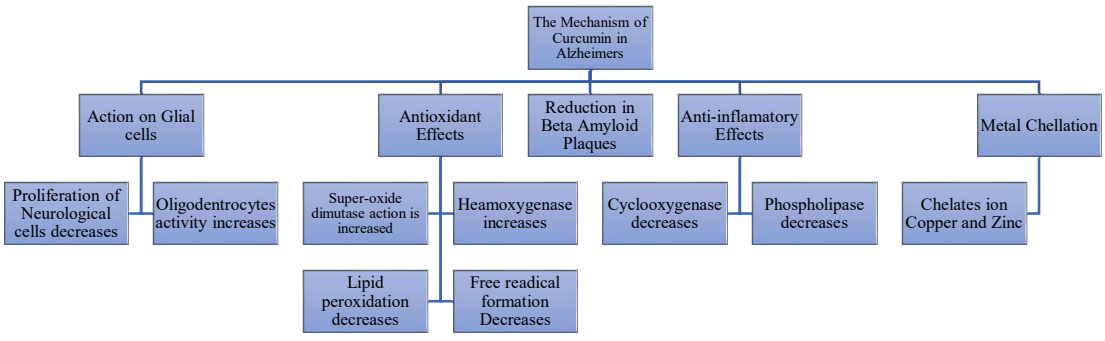

Figure 1: Mechanism of Action of Curcumin in Alzheimer's

(a) Action of Curcumin on Glial cells

The recent histological investigations have shown that the A-beta plaques in the brains of AD patients are surrounded by reactive astrocytes and activated microglia. Chronic microglial activation releases cytokines and other reactive molecules that aggravate A-Beta disease. Therefore, neuroglia plays a significant role in the etiology of AD. Because curcumin is lipophilic and may cross all cell membranes, it has an intracellular impact. On microglia, curcumin exerts anti-proliferative effects. Curcumin has an impact on neuroglial differentiation and proliferation even at low doses. **[21]**

(b) Action of Curcumin as an Antioxidant in Alzheimer's

Scientists have analyzed that curcumin's potent anti-inflammatory and antioxidant qualities help to reduce Alzheimer's symptoms brought on by oxidation. **[22]** According to research it has been observed that the use of curcumin significantly reduced lipo-peroxidation and accumulation of lipofusion, which typically increases with age. **[23]** The sodium-potassium ATPase superoxide dismutase, whose activity typically declines with age, was also activated more. In different investigations, it was shown that curcumin works through the antioxidant route to defend cells from A-beta injury **[24]**. Curcumin guards against several forms of oxidative damage in the brain by mitochondria. Curcumin pre-treatment shields brain mitochondria against peroxynitrite, a strong and flexible oxidant that may target a variety of cells in vitro by direct detoxification and in vivo by increasing total cellular glutathione levels. Peroxynitrite is produced when nitric oxide and superoxide react **[25]**.

(c) Reduction Beta-Amyloid Plaques

The existence of beta-amyloid plaques is the most apparent indication of Alzheimer's Disease. These plaques primarily consist of aggregates of beta-amyloid fibrils, which are minuscule fibers. Inhibiting Abeta production, impeding A-beta fibril formation, and disrupting pre-formed A-beta could represent a promising therapeutic approach for addressing Alzheimer's disease, given that the accumulation of beta-amyloid protein is consistent pathological hallmark in AD-affected brains **[26]**. When the mice were administered with various doses of AD and the one that received the modest dosages of the herb had a 40% reduction in beta-amyloid levels. Low dosages of curcumin also led to a 43% reduction in the "plaque load". Unexpectedly modest amounts of curcumin administered over a longer time period were highly effective than the large doses in halting AD's neurodegenerative process, as the Curcumin interacts to amyloid beta and prevents its self-assembly at greater concentrations **[27]**.

(d) Action of Curcumin as an Anti-Inflammatory in Alzheimer's

It has been discovered that curcumin blocks the transcription factor, phospholipases, cyclooxygenase (COX-2), and enzymes responsible for turning membrane phospholipids into prostaglandins. The pro-inflammatory cytokines TNF (tumour necrosis factor)-alpha and IL (interleukin)-1 beta are inhibited by decreasing the generation of ROS by activated neutrophils, inhibiting AP-1, and blocking NF-Kappa B **[15, 16]**. Overall, curcumin reduces the production of inflammatory cytokines and the key molecule that causes inflammation **[28]**. The intracellular expression of IL-12 p40/p70 and IL-12 p70 is inhibited by curcumin. Additionally, curcumin exposure reduced the amount of cytokines that promote inflammation (IL-1, IL-6, and TNF-). These findings show that curcumin is an effective inhibitor of the generation of pro-inflammatory cytokines, and that this inhibitory effect may vary depending on the kind of target cells **[29]**.

(e) Metal Chelation

By interacting with heavy metals like lead and cadmium, curcumin inhibits the neurotoxicity that is brought on by these metals. It was found that the intraperitoneal injection of lead acetate in rats was examined under a microscope while curcumin was present. According to the data, rats given curcumin injections had much less led-induced neuronal damage **[30]**. Based on the research done at the Chinese University of Hong Kong, curcumin successfully binds to zinc, iron, and copper using spectrophotometry. Additionally, compared to redox-inactive zinc, curcumin bonds more strongly with redox-active metals like copper and iron. Curcumin may inhibit inflammatory damage by blocking the metal's activation of NF-kappa **[31]**.

Treatment of Diabetic Neuropathy by Curcumin

Since there is currently no direct therapy that may directly operate on inflamed neurons to cure them, neuropathic pain is extremely traumatizing and dependent on painkillers for treatment. Despite knowledge of their negative side effects, it is nevertheless extremely usual to utilize indirect treatments to treat degenerating neurons **[32]**. To avoid the condition from getting worse, controlling the sugar level is a key component of treatment; without it, no amount of painkillers or other medications will prove beneficial. Antidepressants, anticonvulsants, and opioids are currently prescribed medications that are used to help counteract the impacts of hyperglycaemia when used with insulin or other hypoglycaemic medications **[33]**. However, using these medications for an extended period of time is a dubious practice and should be avoided. Finding a drug that can

simultaneously decrease blood glucose levels, target all pathogenic glucose events, and prevent the progression of further diabetes problems is therefore extremely important **[34]**. Hyperglycaemia increases the thickness of the wall and hyalinization of the nerve vessel is done that causes microvascular damage in the nerves which leads to nerve ischemia. It also leads to the loss of multifocal fibres located at proximal and distal segments due to this demyelination of nerves takes place. It lets the plasma proteins penetrate capillary membranes to endoneurium that increases pressure and hypoxia and leads to increased thombus formation **[35]**.

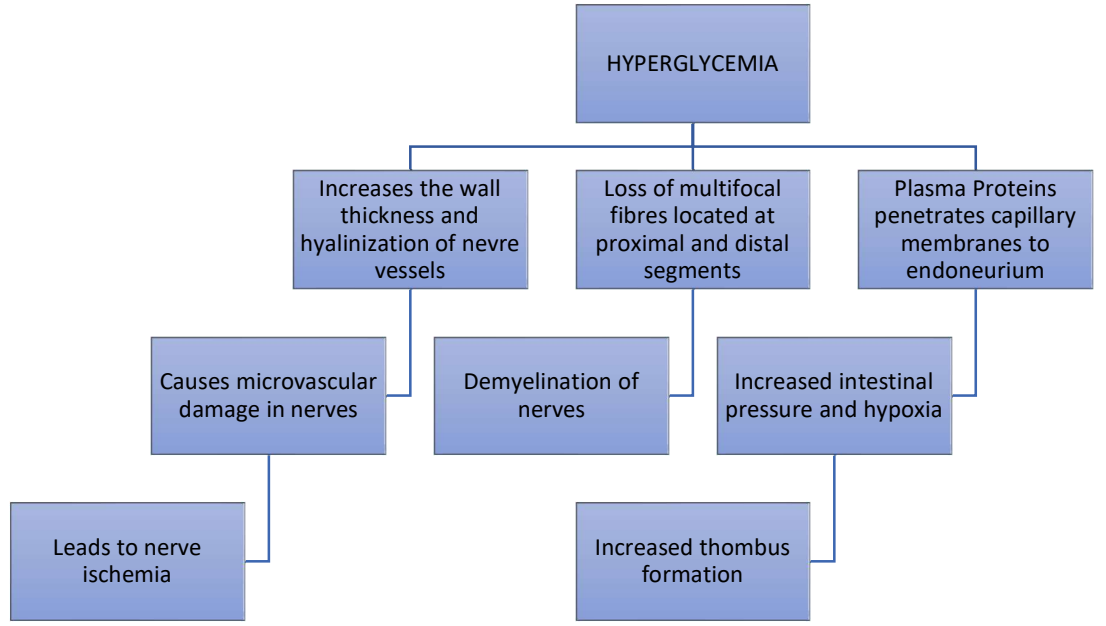

Figure 2: Effect of Hyperglycaemia on Diabetic Patient

The curcumin plant has been linked to a variety of pharmacological effects, but more research is needed to understand how these effects work and what phytochemical components are involved. In the current study, several ideas have been described to anticipate its positive impact in reducing hyperglycaemia **[36]**. It is discovered that the diabetic patients have been observed to suffer with depression and anxiety, that can be cured with the help of curcumin. Additionally, curcumin is identified to reduce oxidative stress in diabetic patients. Curcumin possess tremendous antifungal and antibacterial properties which are discussed in next sections **[34]**.

(a) Action of *Curcuma caesia* in Depression of Diabetic Patients

Anxiety, sleeplessness, mania, and stress all enhances the central nervous system depression. The two most prevalent mental diseases today are anxiety and stress, and the majority of people experience these conditions at some point in their lives. It is

also the most prevalent symptoms seen in diabetic neuropathy patients, who frequently go without even the most basic medical care **[37]**. Tannic acid, a flavonoid and tannic acid-containing component of the herbal remedy *C. caesia* has demonstrated an elevation in the levels of monoaminergic neurotransmitters in the brain by acting as a non-selective inhibitor of monoamine oxidase.

Tyrosine or dopamine level regulation is another route for this action that has been recognized. As a result, psychological stress can be decreased and adrenaline concentrations could potentially assist in the reduction of stress. Due to the lower levels of 5-hydroxytryptophan, it exhibits both CNS depressive and muscle-relaxing properties (5HT) **[38]**. In addition to the modulation mentioned above, it also inhibits cumulative Ca^{2+}-induced contractions that are dependent and non-competitive in the depolarized aorta. As a result, it could prevent the entry of Ca^{2+} ions through VOCCs that have been opened by 60 mM KCl. We may speculate, based on the aforementioned modes of action that its obstruction in conduction can be employed to reduce stress and anxiety as well as delay the development of neuropathic pain and the CNS depressive characteristic **[39]**.

(b) Action *of Curcuma caesia* in Reduction Oxidative Stress

In addition to phenolics and flavonoids, curcumin also has anti-superoxide radicals and anti-singlet oxygen properties **[40]**. Tetrahydro curcumin, one of Curcumin's primary metabolites, has the strongest antioxidant properties of naturally occurring curcuminoids. Curcuminoids have the ability to prevent hydroxyl radicals from damaging supercoiled plasmid DNA. It was determined that curcumin, a well-known powerful antioxidant, is not as effective in trapping the DPPH radical as bis-demethoxycurcumin and demethoxycurcumin **[41]**. Due to the above-mentioned characteristics, *C. caesia* can be employed as a powerful antioxidant, slowing the evolution of diabetes. If used as a preventative measure, it may also be advantageous in the development of the illness and its accompanying complications, such as neuropathy **[42]**.

(c) Anti-fungal And Anti-microbial Properties of *Curcuma caesia in diabetic patient*

Strong antibacterial, antifungal, and cidal properties are displayed by *Curcuma caesia* . It exhibits a protective effect against a range of both Gram-positive and Gram-negative bacteria, in addition to the fungal infection brought on by *C. albicans* **[43]**. The root's methanolic extract and the plant's crude protein show bactericidal and fungicidal properties. The greater defense provided by its phytoconstituents can serve

to lower the steadily rising number of foot amputations **[44]**.

Treatment of Cancer

Researchers are now focusing their efforts on developing organically derived substances for cancer therapy. These organic or natural products have increased safety and possess minimal adverse effects. Medicinal herbs are a plentiful source of this kind of chemicals. Using a mouse model, Hadem *et al*. (2014) investigated the chemo preventive properties of *C. caesia* **[45]**. The BALB/c (model name of mice) mice were subjected to the well-known carcinogen diethyl nitrosamine, which is frequently employed as a hepatocarcinogen inducer, and it was demonstrated that the structural damage brought on by exposure to diethyl nitrosamine may be repaired by a methanolic extract of the *C. caesia* rhizome **[46]**. Furthermore, *C. caesia* hexane rhizome extracts have been proven to inhibit the development of cancer. Numerous apoptotic changes, such as membrane zeosis and the formation of apoptotic bodies, were noticed in cancer cells treated with Western blot analysis and hexane extract. It provided strong evidence that hexane rhizome extracts cause apoptosis by an activated mitochondrial pathway as evidenced by the expression of proapoptotic protein **[47]**. Because these investigations have shown that *C. caesia* has the capacity to prevent cancer cell multiplication, more analysis of the process and kind of cell death induced by its components is proposed. The cytotoxicity of the chemicals must also be investigated further in order to identify the molecular pathway associated with the anticancer capabilities of this valuable medicinal herb.

CONCLUSION:

The current review focuses on the herb *Curcuma caesia* Roxb which is also referred to as black turmeric and has many uses and has great importance in various regions of India. This paper proved that herbal products can be as beneficial as today's treatment and are also regarded to be safer than synthetic products. The paper explained about the utilization of *C. caesia* useful in curing a variety of illnesses and health issues. The rhizomes of the herb have many bioactive characteristics. It has all the required properties that can help in curing Alzheimer's, amnesia, diabetes, anxiety, and depression. *C. caesia* possesses biological properties such as central nervous system depressant, antibiotic, antioxidant property, muscle relaxant, etc. This review paper validates *Curcuma caesia 's* potential as an important medicinal herb which can be a commercially viable product.

REFERENCE:

[1] Nadkarni, K. M. (1976). Indian Materia Medica Popular Prakashan Private Limited.

[2] Anonymous, The wealth of India. Vol.2 New Delhi: Council of Scientifi c and Industrial Research; 2001. P. 264. (n.d.).

[3] Paliwal, P., Pancholi, S. S., & Patel, R. K. (2011). Pharmacognostic parameters for evaluation of the rhizomes of *Curcuma caesia*. *Journal of advanced pharmaceutical technology & research*, *2*(1), 56.

[4] https://www.iiaasd.com/kali-haldi/#:~:text=Black%20turmeric%20is%20native%20to,across%20India%20and%20Southeast%20Asia.

[5] Sarangthem, K., & Haokip, M. J. (2010). Bioactive components in *Curcuma caesia* Roxb. grown in Manipur. *Bioscan*, *5*(1), 113-115.

[6] Sarangthem, K., & Haokip, M. J. (2010). Bioactive components in *Curcuma caesia* Roxb. grown in Manipur. *Bioscan*, *5*(1), 113-115.

[7] Karmakar, I., Dolai, N., Suresh Kumar, R. B., Kar, B., Roy, S. N., & Haldar, P. K. (2013). Antitumor activity and antioxidant property of *Curcuma caesia* against Ehrlich's ascites carcinoma bearing mice. *Pharmaceutical biology*, *51*(6), 753-759.

[8] Jouyban, A., Chan, H. K., & Foster, N. R. (2002). Mathematical representation of solute solubility in supercritical carbon dioxide using empirical expressions. *The Journal of supercritical fluids*, *24*(1), 19-35.

[9] Michielin, E. M., Bresciani, L. F., Danielski, L., Yunes, R. A., & Ferreira, S. R. (2005). Composition profile of horsetail (*Equisetum giganteum* L.) oleoresin: comparing SFE and organic solvents extraction. *The Journal of supercritical fluids*, *33*(2), 131-138.

[10] Borah, S., Sarkar, P., & Sharma, H. K. (2021). Analysing *Curcuma caesia* fractions and essential oil for neuroprotective potential against anxiety, depression, and amnesia. *3 Biotech*, *11*(5), 240.

[11] Kimura, J. (2013). Electrodiagnosis in diseases of nerve and muscle: principles and practice.

[12] Bhattacharya, P., & Patel, T. N. (2021). A study of deregulated MMR pathways and anticancer potential of curcuma derivatives using computational approach. *Scientific reports*, *11*(1), 1-21.

[13] Wojdyło, A., Oszmiański, J., & Czemerys, R. (2007). Antioxidant activity and phenolic compounds in 32 selected herbs. *Food chemistry*, *105*(3), 940-949.

[14] Gazzaniga, M., Ivry, R., & Mangun, G. (2009) Cognitive Neuroscience: The biology of the mind. New York: W.W. Norton & Company.

[15] Lerner, K. L., & Lerner, B. (2003). Gale Encyclopedia of Science.

[16] World Health Organization. (2020). Dementia fact sheet World Health Organization. *Geneve, Switzerland: WHO Press. [Google Scholar]*.

[17] Simon RP, Greenberg DA, Aminoff MJ (2018). Clinical neurology (Tenth ed.). [New York]: McGraw Hill. p. 111.

[18] Knopman DS, Amieva H, Petersen RC, *et al*. (May 2021). "Alzheimer disease". Nat Rev Dis Primers. 7 (1): 33. doi:10.1038/s41572-021-00269-y. PMC 8574196

[19] Francis *et al*. 1999; Zhao and Zhao 2013; Garry *et al*. 2015.

[20] Mishra, S., & Palanivelu, K. (2008). The effect of curcumin (turmeric) on Alzheimer's disease: An overview. *Annals of Indian Academy of Neurology*, *11*(1), 13.

[21] NIDDK. U.S. Department of Health and Human Services. National Institutes of Health NIH Publication No. 09–3185 February 2009.

[22] Frautschy, S. A., Hu, W., Kim, P., Miller, S. A., Chu, T., Harris-White, M. E., & Cole, G. M. (2001). Phenolic anti-inflammatory antioxidant reversal of Aβ-induced cognitive deficits and neuropathology. *Neurobiology of aging*, *22*(6), 993-1005.

[23] Bala, K., Tripathy, B. C., & Sharma, D. (2006). Neuroprotective and anti-ageing effects of curcumin in aged rat brain regions. *Biogerontology*, *7*, 81-89.

[24] Kim, D. S., Park, S. Y., & Kim, J. Y. (2001). Curcuminoids from Curcuma longa L. (Zingiberaceae) that protect PC12 rat pheochromocytoma and normal human umbilical vein endothelial cells from βA (1–42) insult. *Neuroscience letters*, *303*(1), 57-61.

[25] Mythri, R. B., Jagatha, B., Pradhan, N., Andersen, J., & Bharath, M. S. (2007). Mitochondrial complex I inhibition in Parkinson's disease: how can curcumin protect mitochondria?. *Antioxidants & redox signaling*, *9*(3), 399-408.

[26] Scapagnini, G., Foresti, R., Calabrese, V., Stella, A. G., Green, C. J., & Motterlini, R. (2002). Caffeic acid phenethyl ester and curcumin: a novel class of heme oxygenase-1 inducers. *Molecular pharmacology*, *61*(3), 554-561.

[27] Yang, F., Lim, G. P., Begum, A. N., Ubeda, O. J., Simmons, M. R., Ambegaokar, S. S., ... & Cole, G. M. (2005). Curcumin inhibits formation of amyloid β oligomers and fibrils, binds plaques, and reduces amyloid in vivo. *Journal of Biological Chemistry*, *280*(7), 5892-5901.

[28] Park, S. Y., & Kim, D. S. (2002). Discovery of natural products from

Curcuma l onga that protect cells from beta-amyloid insult: A drug discovery effort against Alzheimer's disease. *Journal of natural products*, *65*(9), 1227-1231.

[29] Kim GY, Kim KH, Lee SH, Yoon MS, Lee HJ, Moon DO. (2005) Curcumin inhibits immunostimulatory function of dendritic cells: MAPKs and translocation of NF-B as potential targets. J Immunol, 174:8116–24.

[30] Daniel, S., Limson, J. L., Dairam, A., Watkins, G. M., & Daya, S. (2004). Through metal binding, curcumin protects against lead-and cadmium-induced lipid peroxidation in rat brain homogenates and against lead-induced tissue damage in rat brain. *Journal of inorganic biochemistry*, *98*(2), 266-275.

[31] Baum, L., & Ng, A. (2004). Curcumin interaction with copper and iron suggests one possible mechanism of action in Alzheimer's disease animal models. *Journal of Alzheimer's disease*, *6*(4), 367-377.

[32] Jeong, G. S., Oh, G. S., Pae, H. O., Jeong, S. O., Kim, Y. C., Shin, M. K., ... & Chung, H. T. (2006). Comparative effects of curcuminoids on endothelial heme oxygenase-1 expression: ortho-methoxy groups are essential to enhance heme oxygenase activity and protection. *Experimental & molecular medicine*, *38*(4), 393-400.

[33] Calabrese, V., Butterfield, D. A., & Stella, A. M. (2003). Nutritional antioxidants and the heme oxygenase pathway of stress tolerance: novel targets for neuroprotection in Alzheimer's disease. *The Italian journal of biochemistry*, *52*(4), 177-181.

[34] Grover, M., Shah, K., Khullar, G., Gupta, J., & Behl, T. (2019). Investigation of the utility of *Curcuma caesia* in the treatment of diabetic neuropathy. *Journal of Pharmacy and Pharmacology*, *71*(5), 725-732.

[35] Shukla, P. K., Khanna, V. K., Khan, M. Y., & Srimal, R. C. (2003). Protective effect of curcumin against lead neurotoxicity in rat. *Human & Experimental Toxicology*, *22*(12), 653-658.

[36] Walle, T. (2004). Absorption and metabolism of flavonoids. *Free radical biology and medicine*, *36*(7), 829-837.

[37] Ishii, K., Chang, B., Kerwin Jr, J. F., Huang, Z. J., & Murad, F. (1990). Nω-nitro-L-arginine: a potent inhibitor of endothelium-derived relaxing factor formation. *European journal of pharmacology*, *176*(2), 219-223.

[38] Sultana, N., Azhar, I., & Kabir, A. (2013). Experimental evaluation of ethanol extract of *Curcuma caesia*

Roxb. on locomotor and learning behavior. *Int J Biol Res*, *1*, 123-127.

[39] Murray, M. A., Boyle, J. P., & Small, R. C. (1989). Cromakalim-induced relaxation of guinea-pig isolated trachealis: antagonism by glibenclamide and by phentolamine. *British journal of pharmacology*, *98*(3), 865-874.

[40] Das, K. C., & Das, C. K. (2002). Curcumin (diferuloylmethane), a singlet oxygen (1O2) quencher. *Biochemical and biophysical research communications*, *295*(1), 62-66.

[41] Reddy, A. C. P., & Lokesh, B. R. (1994). Studies on the inhibitory effects of curcumin and eugenol on the formation of reactive oxygen species and the oxidation of ferrous iron. *Molecular and cellular biochemistry*, *137*, 1-8.

[42] Ruby, A. J., Kuttan, G., Babu, K. D., Rajasekharan, K. N., & Kuttan, R. (1995). Anti-tumour and antioxidant activity of natural curcuminoids. *Cancer letters*, *94*(1), 79-83.

[43] Pandey, D., & Gupta, A. K. (2014). Antibacterial efficacy of *Curcuma caesia* from Bastar district of Chhattisgarh, India. *International Journal of Pharmaceutical Sciences and Research*, *5*(6), 2294.

[44] Mannangatti, K. (2008). Antifungal protein from a medicinal plant, *Curcuma caesia* Roxb. *Journal of Biotechnology*, *136*, S90.

[45] Greenwell, M., & Rahman, P. K. S. M. (2015). Medicinal plants: their use in anticancer treatment. *International journal of pharmaceutical sciences and research*, *6*(10), 4103.

[46] Mukunthan, K. S., Anil Kumar, N. V., Balaji, S., & Trupti, N. P. (2014). Analysis of essential oil constituents in rhizome of *Curcuma caesia* Roxb. from South India. *Journal of Essential Oil Bearing Plants*, *17*(4), 647-651.

[47] Hadem, K. L. H., Sharan, R. N., & Kma, L. (2014). Inhibitory potential of methanolic extracts of Aristolochia tagala and *Curcuma caesia* on hepatocellular carcinoma induced by diethylnitrosamine in BALB/c mice. *Journal of carcinogenesis*, *13*.