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Research Article

Neurobehavioral deficits of $AlCl_3$ attenuated by administration of Turmeric supplementation in rats

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Abstract

Turmeric is a very commonly used medicinal plant. Its main phytochemical component is curcumin. It is known to possess a neuroprotective, anti-inflammatory and antihypertensive properties. Dementia has a crucial impact on physical and emotional well-being of patients. It is a clinical syndrome indicated by a gradual decrease in cognitive function which obstruct one's ability to live autonomously. It is widely used in foods and well known about its analgesic effects. Purpose of current study is to know about its effect on brain functions and possible effects on antioxidant mechanism which will be helpful to rule out different possible neuronal disorders. Eighteen rats were taken and divided into three groups control and two tests. Control was given saline while tests were given intraperitoneal (i.p) $AlCl_3$ for 21 days at a dose of 50mg/kg/ml and the second test group was co-treated with orally turmeric 90mg/kg. Memory functions were evaluated by using the Morris water maze test while biochemical test perform using blood samples and brain sample used for antioxidant effects. In Morris water maze test $AlCl_3$administered group shows increase in latency time showing memory impairment that attenuated by turmeric supplement with wound formation in skin. The co-treated group 2 showed improved memory functions and biochemical effects while recovery of wounds also seen. Present study showed that Turmeric can attenuate dementia caused by $AlCl_3$ and healing different wounds. $AlCl_3$ also induced hyperglycemia effect that is attenuated by turmeric administration. Present study suggests that turmeric would be helpful against $AlCl_3$ induced dementia and its prevention.

Keywords: $AlCl_3$; Curcumin; Memory; Wound

Introduction

Turmeric has a medicinal use in different regions of world. Turmeric has above 100 of components which have been extracted from it. The primary active compound in turmeric is curcumin **[1]**. Research robustly suggested that curcumin, the active compound of turmeric is the vital ingredient, responsible for major remedial activities of turmeric **[2]** and its derivatives extracts were found to be bioactive. It has a healing effect on both aseptic and septic wounds in rats and rabbits

[3]. Turmeric has been used in Ayurveda to treat eye infection, burns, acne, wound healing, sprains and inflammation **[4]**. Further scientists reported that traditional medicine utilized turmeric to boost immunity and treat various respiratory ailments like asthma and allergies **[4]**. Since ancient times belief in anti-inflammatory properties of this polyphenol compound has been widely acknowledged **[5]**.

Dementia is described as a clinical syndrome indicated by a gradual decrease in cognitive function which obstruct one's ability to live autonomously **[6]**. Curcumin been found in reduction of oxidative stress, swelling, and cognitive deficits in rats administering Central Nervous System (CNS) infusions of toxic Aβ **[7]**. *In vivo* beta amyloid accumulation may be reduced by curcumin in living organisms due to other activities besides its initial mechanism of directly inhibiting the formation of beta amyloid aggregates. Other additional mechanism like metal binding has been demonstrated to inhibit the amyloid formation **[8]**, the antioxidant vitamin E **[9]**, lowering cholesterol **[10]** and by lowering the activation of an enzymes beta secretase (BACE1) through reduction of its stimulation by IL-1B, (TNF-α) 11 and 4 hydroxynonenal, this is accomplished by suppressing transcription mediated by JNK also referred as stress activated protein kinases(SAPKS) **[11, 12]**. Past studies showed that researchers monitored amyloid plaques in mice with Alzheimer diseases (AD) using in vivo multi photon microscopy. the result postulated that curcumin was able to enter brain, bind to plaques and diminish size of plaque by 30% and reduce Aβ level significantly in living organisms **[13]**. Curcumin's property of healing wounds is due to its biochemical properties, including its anti-inflammatory effects **[14]** anti-infectious and antioxidant **[15]** actions. Curcumin has been revealed to boost skin wound healing by participating in tissue remodelling, granulation, tissue formation, and deposition of collagen **[16]**.

Oxidative stress is associated with many chronic illnesses and its mechanisms are closely linked to inflammation as one can easily trigger off the other. During inflammation It is widely acknowledged that inflammatory cells release different reactive species, causing oxidative stress and emphasizing a connection between oxidative stress and inflammation **[17]**. Moreover, several reactive oxygen/nitrogen species can initiate a signalling cascade in cells that increasing the activation of pro-inflammatory genes. The onset of numerous chronic diseases and conditions are due to inflammation **[18]**. These diseases encompass AD, Parkinson's disease, metabolic syndrome and depression **[18]**. Curcumin has a key role in restraining the diseases by regulation of biological functions. Efficient ability of scavenging reactive oxygen species (ROS) describes its role in cessation of disease causation. They further suggested that curcumin has ability to inhibit inflammation through various processes.

The anti-inflammatory property of curcumin has a crucial role in health management. Even so, the unambiguous way in which curcumin exhibits its anti-inflammatory benefits remains unknown **[19]**. However, it is supposed that curcumin works as an anti-inflammatory by suppressing the activity of enzymes like cyclooxygenase-2 (COX-2) and 5 lipoxygenases **[19]**. Its participation in disease management was accredited through its ability to inhibit disease evolution. Turmeric along with its component curcumin evidenced neuro protective properties, although specific mechanism of action remains unclear.it is believed that the neuroprotective effect of turmeric is attributed to its phenolic compound content **[19]**. Recent a study design to analyse neuro behavioural and biochemical impacts of

administering turmeric and $AlCl_3$ to rats. The phenolic compounds in turmeric are thought to be responsible for its neuroprotective properties. Present research design is to elaborate neurobehavioral and biochemical effects following turmeric and $AlCl_3$ administration in rats.

Materials and Methods

Eighteen locally bred albino Wistar rats purchased from Aga Khan University Hospital Karachi. After bringing they were caged separately in a silent room and maintained light and dark cycles. Animals were habituating at least 3 days before start of experiment. Animals were divided into 3 group, control (treated with saline), Test1 (treated with $AlCl_3$) and Test 2 (co-treated with $AlCl_3$+Turmeric). Behavioural activities were monitored after twenty-one days of drug treatment. After behavioural activity rats were decapitated, blood and brain were collected for biochemical and antioxidant analysis. The procedure was regulated by following the guidelines of National Institute of Health's Guide for Care and Use of Laboratory Animals (Publication No. 85−23, revised 2011). All experiments were performed after the approval of Local Animal Ethical Care Committee.

Behavioural methods:

Morris Water Maze Test

Spatial memory effects assessed by using Morris water maze. Apparatus comprises of a circular tank having opaque water with a hidden platform. Experimentation by Morris water maze test **[20]**.

Antioxidant Estimations

Determination of Catalase (CAT)

Catalase activity is measured using brain sample and reported procedure was followed as in **[21]**. For the filtrate brain tissue used and prepare homogenate in phosphate buffer. Filtrate was taken and mixed H2O2 and phosphate buffer. The % inhibition of catalase was determined, and solutions are read at 620 nm and get absorbance.

Determination of Malondialdehyde (MDA)

MDA estimation in brain sample was done which is reported as according to **[21]**. In a test tube brain homogenate were taken and then proceed to reaction by introducing in a water bath. After cooling the mixture centrifugation done, absorbance was read at 532 nm using supernatant.

Results

The effect of turmeric administration against the $AlCl_3$ on spatial memory shown in (Fig. 1). Data analyzed by One-way ANOVA by Tukey's test showed a significant effect on memory functions ($F = 23.425$, $df = 17$, $p<0.01$). These results show that the effect of $AlCl_3$ significantly impaired ($p<0.01$) the spatial memory as compared to control and turmeric supplementation attenuates significantly and enhanced ($p<0.01$) memory functions in rats as compared to control and $AlCl_3$ treated group.

The effect of Turmeric administration against AlCl3 on plasma glucose level is shown in (Fig. 2). Data analyzed by one-way ANOVA by Tukey's showed a significant effect on plasma glucose levels ($F = 35.34$, $df= 17$, $p<0.01$). These results show that AlCl3 significantly increased ($p<0.01$) the plasma glucose level, Turmeric significantly decreased ($p<0.01$) the plasma glucose levels as compared to control and AlCl3 treated group. This shows that turmeric administration can cause a hypoglycemic effect, while the AlCl3 administration produces a hyperglycemic effect.

The effect of Turmeric administration against the $AlCl_3$ on MDA is shown in (Fig. 3). Data analyzed by One-way ANOVA by Tukey's test showed a significant effect on malondialdehyde levels ($F = 13.21$, $df = 17$, $p<0.01$). These results show that the effect of $AlCl_3$ significantly increased MDA levels ($p<0.01$) as compared to control, and Turmeric significantly decreased the MDA and attenuated effect of $AlCl_3$ ($p<0.01$) in rats as compared to control and $AlCl_3$ treated

group. The effect of Turmeric administration against AlCl3 on catalase activity is shown in (Fig. 4). Data analyzed by One-way ANOVA by Tukey's test showed a significant effect on catalase ($F = 41.2$, $df = 17$, $p<0.01$). These results show that the effect of $AlCl_3$ significantly impaired ($p<0.01$) antioxidant mechanism as compared to control, and Turmeric significantly attenuated ($p<0.01$) effect and decreasing catalase activity in rats as compared to control and $AlCl_3$ treated group.

While (Fig. 5) shows scars as the $AlCl_3$ administration on skin. These scars soon heal after co administration of turmeric. Although turmeric produces its neuro protective and biochemical role as well as physically it heals injuries.

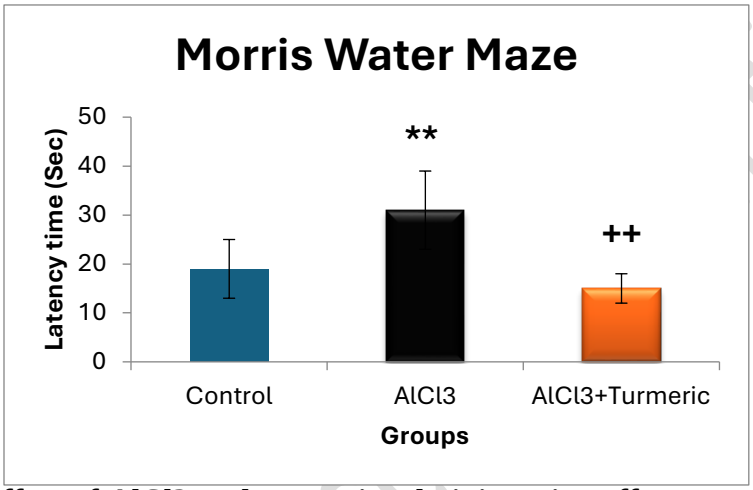

Figure 1: Shows effect of AlCl3 and turmeric administration effects on memory functions. Values show as mean ± SD(n=6) analysis by One-way ANOVArevealed a significant effect **P<0.01vs control, ++P<0.01 vs AlCl3

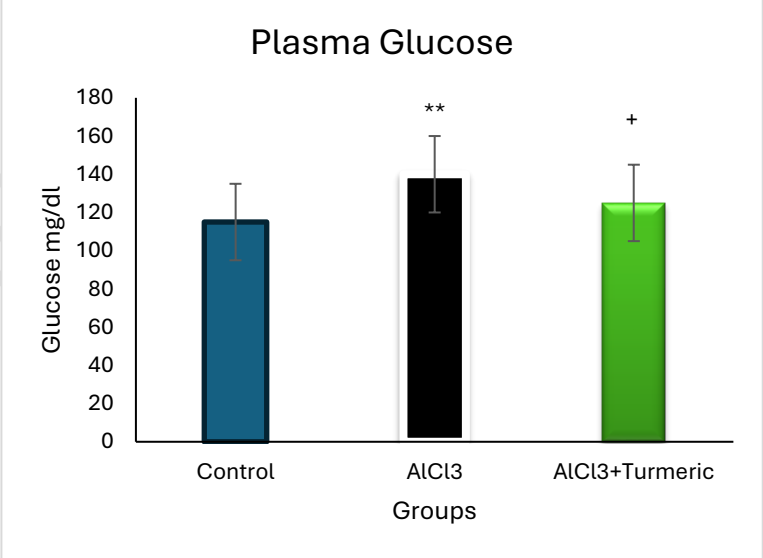

Figure 2: Shows effect of AlCl3 and turmeric administration effects on plasma glucose levels. Values show as mean ± SD(n=6) analysis by One-way ANOVArevealed a significant effect **P<0.01vs control, +P<0.05 vs AlCl3

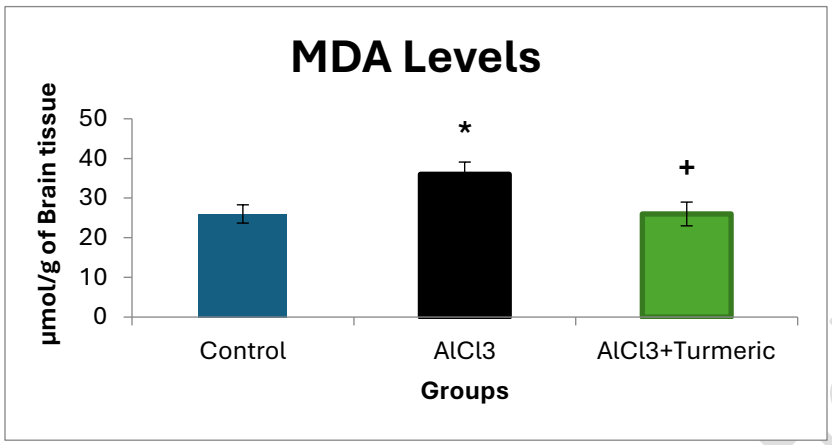

Figure 3: Shows effect of AlCl3 and turmeric administration effects. Values show as mean ± SD(n=6) analysis by One-way ANOVArevealed a significant effect *P<0.05vs control, +P<0.05 vs AlCl3

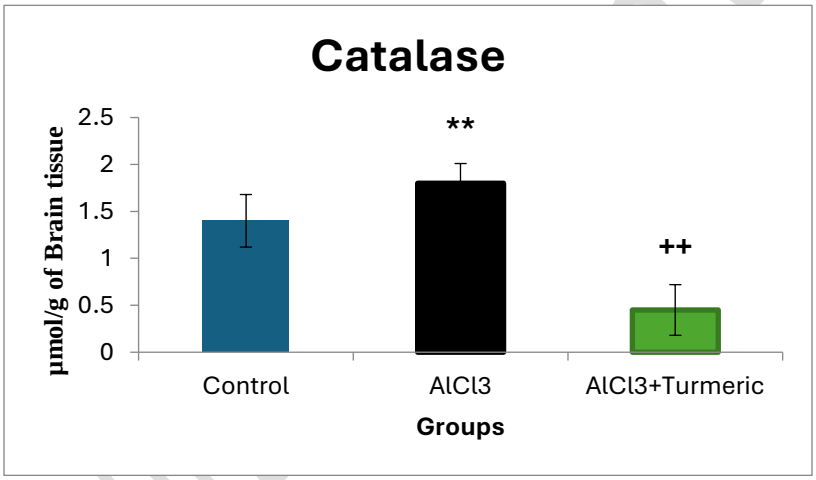

Figure 4: Shows effect of AlCl3 and turmeric administration effects. Values show as mean ± SD(n=6) analysis by One-way ANOVArevealed a significant effect **P<0.01vs control, ++P<0.01 vs AlCl3

Figure 5: Shows healing effects of Turmeric following AlCl3 administration. (A: AlCl3 administration, B: Turmeric effect healing start, C: Complete healing)

Discussion

In the present study the test group was i.p administered anhydrate $AlCl_3$ for twenty-one days at a dose of 50mg/ml/kg. The chronic administration of $AlCl_3$ produced memory impairment represents symptoms of dementia, also it shows impairment in biochemical, antioxidant parameters but with the administration of turmeric all effects get attenuated and improved while injected site injuries also recovered after turmeric supplementation.

Previous studies stated that progression of neurodegenerative disorders including dementia are due to collection of aluminum in the brain **[22]**. Epidemiological research has documented a link between chronic aluminium exposure and cognitive impairment and neurological toxicity **[23]**. Scientists have stated that patients who underwent extended dialysis sessions developed dialysis dementia because of aluminium-containing dialysates, while the exposure of miners to aluminium powder has emerged as a cause of cognitive impairment **[23]**. The current study also reveals that administration of aluminum causes impairment in memory functions as seen in Morris water maze test indicating an increase in latency time. A body of evidence suggests different neurological toxicities associated with aluminum through different oxidative and inflammatory events activations. Animals exposed to aluminum developed dementia-like conditions with features viz., increased levels of Aβ protein development of hyperphosphorylated tau protein **[24]**, degeneration of cholinergic terminals in cortex and hippocampus **[25]**, development of oxidative stress and neuronal apoptosis **[26]**. Scientists **[27]** reported that after long-term exposure, Aluminium can be found in all parts of the rat brain including the hippocampus where memory and learning occur, influencing hippocampal synaptic plasticity.

Present study shows that test group that was co-treated with Turmeric (Curcumin) administered orally at a dose of 90mg/kg and $AlCl_3$ for 21 days at a dose of 50mg/ml/kg for 21 days showed significant improvement in memory functions. In Morris water maze test shows decrease in latency time significantly, thus demonstrating that Turmeric may effective and used to be treated the memory impairment. As per the past research, invitro study shows curcumin has a noticeable restrictive acetylcholine esterase (AchE) activity in hippocampus and frontal cortex of dementia in treated animals and guards against NMDA persuade toxicity **[28]**. In addition, it has been described that activity of choline acetyl transferase can enhanced by curcumin. This enzyme responsible for amalgamating acetylcholine in hippocampus rat models with Alzheimer diseases **[29]**. It has been expressed that curcumin might be effective in preventing and lessening cognitive decline by having anti neuro inflammatory properties and antioxidant as well as balance the cholinergic system **[30]**.

In addition to these behavioral effects, some biochemical effects were also seen in the blood of rats. Glucose levels were tested in the serum of rats after treatment with Turmeric. In this study, the serum glucose level is significantly elevated in the serum of the Test group after treatment as compared to the Control group. This could be because of the impairment with AlCl3. Previous studies show, turmeric is known to have hypoglycemic effect, HBA1c level and blood glucose level can be lowered by curcumin due to lowering in hepatic glucose production ,glycogen synthesis, enhancing gene expression of GLUT4, GLUT2, GLUT3 receptors, activating adenosine monophosphate (AMP) kinase increasing secretion from pancreatic tissues ,increasing functions of pancreatic cell, enhancing phosphorylation of AKT (PKB) and insulin receptor β and lowering insulin resistance

[31]. Although, it didn't produce such an effect on the rats impaired with $AlCl_3$. This could be due to the irreversibility of damage caused by $AlCl_3$. $AlCl_3$ induced oxidative damage is the cause of damage to pancreatic islet which causes increase in blood glucose level and having the property of strong oxygen acceptor and have ability of binding to other oxygen donors produces reactive oxygen species causing oxidative damage **[32]**.

This study showed wound healing effects of curcumin, wounds ranging from 2nd degree to 3rd degree were reduced back to 1st degree and minor scars. Previous studies tell that the curcumin's ability to heal wounds is due to its biochemical actions, including its anti-inflammatory properties **[14]**, anti-infectious and antioxidant **[15]** activities. Curcumin has been revealed to boost skin wound healing by tissue formation their remodelling, granulation, and collagen deposition **[16].** Many studies have revealed that the application of curcumin on wound also increases epithelial regeneration, fibroblast proliferation and vascular density **[33]**.

Conclusion

In conclusion, chronic administration of $AlCl_3$ can cause memory impairment in rats. It also alters the serum levels of Glucose and antioxidant system. Treatment of rats with AlCl3-induced dementia with Turmeric can reverse these effects and improve memory and other symptoms of dementia. It can also decrease the elevated levels of glucose. However, it cannot reverse the hyperglycemic effects caused by $AlCl_3$ which causes hepatotoxic effects. It destroys the islet cells in the pancreas causing necrosis and call damage. This results in irreversible hyperglycemia, which could not be reversed by treatment with Turmeric, and it can reduce the degree of cutaneous wounds, even so much as to turn them into scars.

Authors' contributions

Conceived and designed the experiments: I Sajid & L Anis, Performed the experiments: H Khan & W Qureshi, Analysed the data: SI Hussain, Wrote the paper: S Ahmed & I sajid.

References

1. Betül K & Nevin Ş (2017). Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. *Crit Rev Food Sci Nutr* 57(13): 2889-2895.
2. Pal S & et al. (2001). Mechanisms of curcumin-induced apoptosis of Ehrlich's ascites carcinoma cells. *Biochem Biophys Res Commun* 288: 658–665.
3. Seraw E, Melkamu Y & Masresha G (2024). Traditional lore on the healing effects of therapeutic plants used by the local communities around Simien Mountains National Park, northwestern *Ethiopia. J Ethnobiol Ethnomed* 20(1): 43.
4. Araujo MCP, Antunes LMG & Takahashi CS (2001). Protective effect of thiourea, a hydroxy / radical scavenger on curcumin-induced chromosomal aberrations in an in vitro mammalian cell system. Teratogen. *Carcin Mut* 21: 175–180.
5. Aggarwal BB, Kumar A & Bharti AC (2003). Anticancer potential of curcumin: preclinical and clinical studies. *Anticancer Res* 23: 363–398.
6. Chertkow H, Feldman HH & Jacova C, *et al.* (2013). Definitions of dementia and predementia states in Alzheimer's disease and vascular cognitive impairment: consensus from the Canadian conference on diagnosis of dementia. *Alzheimer's Res Ther* 5(suppl-1): S2.
7. Frautschy SA, Hu W, Miller SA, Kim P, Harris-White ME & Cole GM (2001). Phenolic anti-inflammatory antioxidant reversal of Aβ-induced cognitive deficits and neuropathology. *Neuro Biol Aging* 22: 991–1003.

8. Huang X, Atwood CS, Moir RD, Hartshorn MA, Tanzi RE & Bush AI (2004). Trace metal contamination initiates the apparent auto-aggregation, amyloidosis, and oligomerization of Alzheimer's Abeta peptides. *J Biol Inorg Chem* 9: 954–960.
9. Sung S, Yao Y, Uryu K, Yang H, Lee VM, Trojanowski JQ & Pratico D (2004). Early vitamin E supplementation in young but not aged mice reduces Abeta levels and amyloid deposition in a transgenic model of Alzheimer's disease. *FASEB J* 18: 323–325.
10. Fassbender K, Simons M, Bergmann C, Stroick M, Lutjohann D, Keller P, Runz H, Kuhl S, Bertsch T, von Bergmann K, Hennerici M, Beyreuther K & Hartmann T (2001). Simvastatin strongly reduces levels of Alzheimer's disease beta - amyloid peptides Abeta 42 and Abeta 40 in vitro and in vivo. *Proc Natl AcadSci* USA 98: 5856–5861.
11. Sastre M, Dewachter I, Landreth GE, Willson TM, Klockgether T, van Leuven F & Heneka MT (2003). Nonsteroidal anti-inflammatory drugs and peroxisome proliferator-activated receptor-gamma agonists modulate immunostimulant processing of amyloid precursor protein through regulation of beta-secretase. *J Neurosci* 23: 9796–9804.
12. Tabaton M (2004). Oxidative stress and beta-APP proteolytic processing. *Neurobiol Aging* 25(S2): S69 (S64-02-03).
13. Ruan Y, Xiong Y, Fang W, Yu Q, Mai Y, Cao Z, Wang K, Lei M, Xu J, Liu Y, Zhang X, Liao W & Liu J (2022) Highly sensitive Curcumin-conjugated nanotheranostic platform for detecting amyloid-beta plaques by magnetic resonance imaging and reversing cognitive deficits of Alzheimer's disease via NLRP3-inhibition. *J Nanobiotechnol* 20(1): 322.
14. Liang G, Yang S, Zhou H, Shao L, Huang K, Xiao J & Li, X (2009). Synthesis, crystal structure and anti-inflammatory properties of curcumin analogues. *Eur J of Med Chem* 44(2): 915-919.
15. Meng B, Li J & Cao H (2013). Antioxidant and anti-inflammatory activities of curcumin on diabetes mellitus and its complications. *Curr Pharma Design* 19(11): 2101-2113.
16. Joe B, Vijaykumar M, & Lokesh BR (2004). Biological properties of curcumin-cellular and molecular mechanisms of action. *Critical Rev in Food Sci and Nutr* 44(2): 97-111.
17. Biswas SK (2016). Does the Interdependence between Oxidative Stress and Inflammation Explain the Antioxidant Paradox? *Oxid Med Cell Longev* 5698931.
18. Panahi Y, Alishiri GH, Parvin S & Sahebkar A (2016) Mitigation of systemic oxidative stress by curcuminoids in osteoarthritis: Results of a randomized controlled trial. *J Diet Suppl* 13: 209–220.
19. Rahmani, Arshad Husain, Alsahli, Mohammed A. Aly, Salah M.; Khan, Masood A, Aldebasi & Yousef H (2016) Role of Curcumin in Disease Prevention and Treatment 2. *Adv Biomed Res* 7(1): 38, .
20. Kawahara, M. (2005). Effects of aluminum on the nervous system and its possible link with neurodegenerative diseases. *J of Alzheimer's Dis* 8(2): 171–182.
21. Chatterjee K, Mazumder PM & Banerjee S (2023).Vitamin K2 protects against aluminium chloride-mediated neurodegeneration. *Inflammopharmacol* 31(5): 2675-2684.
22. Walton JR (2007). An aluminum-based rat model for Alzheimer's disease exhibits oxidative damage, inhibition of PP2A activity, hyperphosphorylated tau,

and granulovacuolar degeneration. *J of Inorg Biochem*101(9): 1275-1284.
23. Arab-Nozari M, Zamani E, ALatifi & Shaki F (2019). Mitochondrial toxicity of aluminium nanoparticles in comparison to its ionic form on isolated rat brain mitochondria. *BratislLekListy* 120(7): 516-522.25
24. Niu Q, Yang Y, Zhang Q, Niu P, He S, Gioacchino M, & Boscolo P (2007). The relationship between Bcl-2 gene expression and learning & memory impairment in chronic aluminum-exposed rats. *Neurotoxicity Res* 12(3): 163-169.
25. Ahmed T & Gilani AH (2009). Inhibitory effect of curcuminoids on acetylcholinesterase activity and attenuation of scopolamine-induced amnesia may explain medicinal use of turmeric in Alzheimer's disease. *Pharmacol Biochem Behav* 91(4): 554-559.
26. Singh S, Agrawal N & Goyal A (2024). Role of Alpha-7-Nicotinic Acetylcholine Receptor in Alzheimer's Disease. *CNS NeurolDisord Drug* Targ.
27. Yadav RS, Chandravanshi LP, Shukla RK, Sankhwar ML, Ansari RW & Shukla PK, *et al*. (2011). Neuroprotective efficacy of curcumin in arsenic induced cholinergic dysfunctions in rats. *Neurotoxicol* 32: 760–768.
28. Ghorbani Z, Hekmatdoost A, & Mirmiran P (2014). Anti-hyperglycemic and insulin sensitizer effects of turmeric and its principal constituent curcumin. *Inter J of Endocrino and Metabol* 12(4).
29. Masahiro K & Midori KN (2011). Link between Aluminum and the Pathogenesis of Alzheimer's Disease: The Integration of the Aluminum and Amyloid Cascade Hypotheses. *Int J Alzheimers Dis* 276393.
30. Nampoothiri M, John J, Kumar N, Mudgal J, Nampurath GK, & Chamallamudi, MR (2015). Modulatory role of simvastatin against aluminium chloride-induced behavioural and biochemical changes in rats. *Behavioural Neurol*.
31. Srinivasan K, Sambaiah K, & Chandrasekhara N. (2004). Spices as Beneficial Hypolipidemic Food Adjuncts: A Review. *Food Rev Inter* 20(2): 187–220.
32. Ramírez-Tortosa MC, Mesa MD, Aguilera MC, Quiles JL, Baró L, Ramirez-Tortosa CL, Martinez-Victoria E & Gil A (1999). Oral administration of a turmeric extract inhibits LDL oxidation and has hypocholesterolemic effects in rabbits with experimental atherosclerosis. *Atherosclerosis* 147(2): 371-378.
33. Thangapazham RL, Sharad S & Maheshwari RK (2013). Skin regenerative potentials of curcumin. *Biofactors* 39(1): 141-149 36.