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REVIEW ARTICLE **OPEN ACCESS**

THE IMPACT OF ADDITIONAL GINKGO BILOBA EXTRACT ON COGNITIVE FUNCTION IN ACUTE ISCHEMIC STROKE: A SYSTEMATIC REVIEW AND META ANALYSIS

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ABSTRACT

Background: Stroke is the primary cause of mortality and disability among patients worldwide, and can cause cognitive impairment among these patients. Ginkgo Biloba Extract is an organic compound made from G. Biloba. The active ingredients in Ginkgo biloba extract have demonstrated some clinical benefits for cognitive impairment.
Objective: We aim to investigate whether the addition of Ginkgo Biloba Extract to patients with acute ischemic stroke improves their cognitive function after follow-up.
Methods: A literature search was conducted on PubMed, Google Scholar, and the Cochrane Database, without publication date limits, to identify studies investigating the effect of Ginkgo Biloba Extract on the cognitive function of patients with Acute Ischemic Stroke. The study's primary outcome is a change in cognitive status compared with the baseline, which was assessed with the Montreal Cognitive Assessment (MoCA) after follow-up.
Results: Four randomized controlled trials with 3824 patients were identified. Based on the analysis, the addition of Ginkgo Biloba Extract had a significant impact on improving the MoCA score of acute ischemic stroke patients (MD = 0.47 [0.45-0.49], I2 = 76%, p < 0.00001).
Conclusion: Additional Ginkgo biloba extract may improve cognitive function in patients with acute ischemic stroke.

Keywords: acute ischemic stroke, cognitive function, ginkgo biloba, Montreal Cognitive Assessment, systematic review

Introduction

Stroke, or cerebrovascular accident (CVA), is defined as the dysfunction of the brain due to a disturbance of the cerebral blood flow, and is the second most common cause of death and adult disability around the world.[1] There are about 30% of patients suffering from stroke who experience residual disabilities, and it has been confirmed that stroke can result in cognitive impairment.[2]

Ginkgolide-related intravenous preparation is a class of multitargeted neuroprotectants widely used for the treatment of cardiocerebrovascular diseases in China, primarily composed of ginkgolide A (GA, 1.6 mg/mL), ginkgolide B (GB, 2.9 mg/mL), and ginkgolide K (GK, 0.19 mg/mL). It is a patented Chinese medicine certified by the State Pharmaceutical Administration of China (SPAC) for the treatment of mild to moderate cerebral infarction.

Previous studies have identified a variety of mechanisms that might contribute to the neuroprotective effects of ginkgoid components, with increasing cerebral blood flow, inhibition of inflammation with reductions in the levels of nuclear

factor kappa-B, tumor necrosis factor-alpha, interleukin-beta-1, interleukin-6 and other inflammatory mediators, down-regulation of JNK1/2 and p38 MAPK signaling pathways, decreased production of reactive oxygen species and anti-oxidative actions, attenuation of mitochondrial dysfunction, suppression of neurotransmitter release and excitotoxicity, up-regulation of brain-derived neurotrophic factor, modulation of metabolic pathways, alteration of the phenotype of microglia/macrophages, protection of blood-brain barrier integrity, enhanced astrocyte viability/activity and secretion of erythropoietin and activation of pathways involving heme oxygenase-1.[5]

The two main active components of GDLI, GB (60%) and GK (2%), were reported to be potent and specific inhibitors of platelet-activating factor (PAF), which can activate platelet function and induce thrombus formation.[6] Animal studies showed that the cognitive functions were superior in ginkgo biloba L. leaf extract-treated mice after cerebral artery occlusion.[6] Randomized, placebo-controlled trials have demonstrated that Ginkgo Biloba Extract improved cognitive performance in patients with age-associated mild impairment in cognitive function, vascular dementia, and Alzheimer's disease.[7,8] Therefore, adding Ginkgo Biloba Extract might improve cognitive function in post-stroke cognitive impairment.

Methods

1. Search and Study Selection

This study was a systematic review and meta-analysis. The literature search was done through PubMed without publication date limits to identify the effects of the addition of Ginkgo Biloba Extract on Cognitive Function in the Acute Ischemic Stroke Population with these keywords: ("Acute Ischemic Stroke") and (Ginkgo Diterpene Lactone Meglumine or Ginkgolides or Ginkgo Biloba) and ("Cognitive Function").

The process of study selection encompassed two stages. Initially, two reviewers screened titles and abstracts. Subsequently, in cases where abstracts lacked clarity, the full-text articles of selected studies were obtained and reviewed. The third author contributed to the writing and provided a broader perspective on the research. Data extraction was performed using an Excel spreadsheet, which encompassed details such as author, publication year, participant characteristics, and recorded outcomes.

2. Type of Intervention

The interventions described in selected articles included adding Ginkgo biloba extract, either alone or in combination with conventional stroke therapy. The primary outcome of this study is the proportion of patients with increased MoCA scores from baseline after follow-up.

3. Data Extraction and Analysis

The articles were collected using the PRISMA diagram and critically appraised using PICO analysis (Figure 1). The risk of bias for each study was assessed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (Figure 2).[11] The data were analyzed using Review Manager 5.4.1 software with a Fixed Effect Model.

Results

The initial search yielded 97 articles. After removing duplicates, irrelevant articles, literature reviews, systematic reviews, and meta-analyses, we identified four randomized controlled trials (RCTs) that investigated the effect of Ginkgo Biloba extract on cognitive function, as assessed by the MoCA score, in patients with Acute Ischemic Stroke.

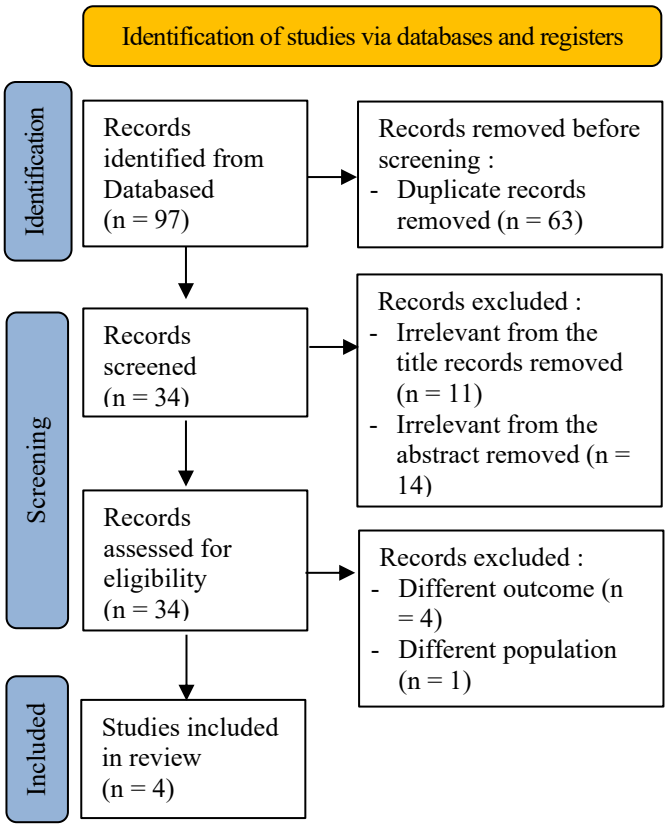

Figure 1. PRISMA diagram

We identified four randomized controlled trials with a total of 3824 patients. These trials compared the functional outcome after the addition of Ginkgo Biloba extract. The characteristics of the included studies are depicted below (Table 1). Qiang Dong et al.'s study reported adequate randomization using a validated computer program (SAS macro RANSC), which an independent member of the biometrics department performed. Xia Meng et al.'s study randomization number was generated centrally by an independent statistician.[10,11]

Table 1. Characteristics of the included studies

Author (Year)	Country	Age	Intervention Arm	Follow Up
Qiang Dong (2023)	China	55-71 yrs	EGb 761	24 weeks
Xia Meng (2024)	China	41-92 yrs	GDLM 25mg	90 days
Liu (2024)	China	50-80 yrs	GDLM 25mg	6 months
Li (2017)	China	18-80 yrs	GBE+Aspirin	180 days

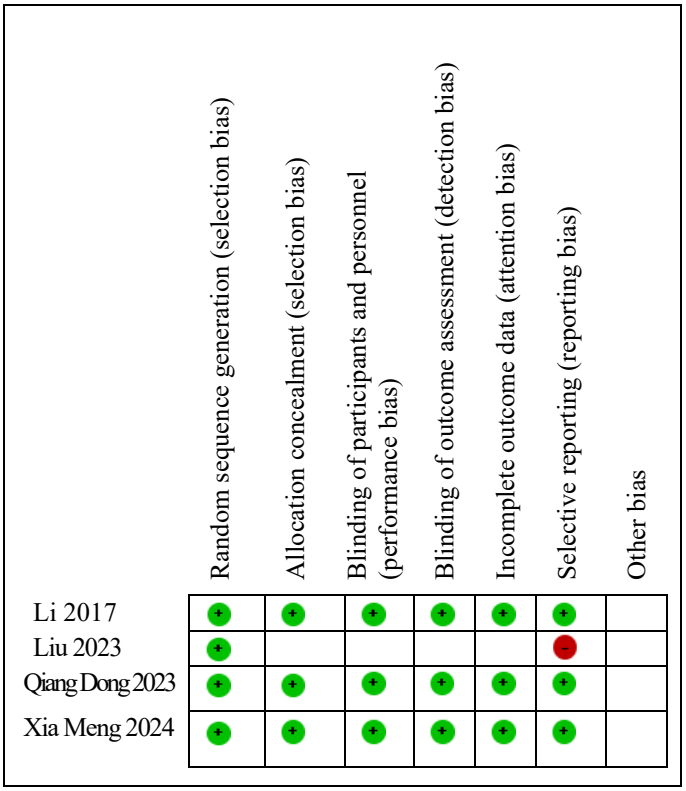

Figure 2. Risk of Bias

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Qiang Dong 2023	2.92	3.9	97	1.33	3.75	96	0.1%	1.59 [0.51, 2.67]	2023
Xia Meng 2024	5.51	0.35	1588	5.04	0.35	1575	99.9%	0.47 [0.45, 0.49]	2024
Total (95% CI)			**1685**			**1671**	**100.0%**	**0.47 [0.45, 0.49]**	

Heterogeneity: $Chi^2 = 4.13$, df = 1 (P = 0.04); $I^2 = 76\%$
Test for overall effect: Z = 37.82 (P < 0.00001)

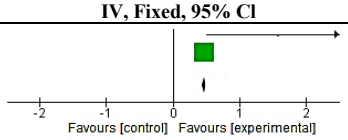

Figure 3. Forrest Plot of Changes in MoCA score after follow-up

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Qiang Dong 2023	0.88	1.42	97	0.17	1.39	96	0.0%	0.71 [0.31, 1.11]	2023
Xia Meng 2024	0.94	0.12	1588	0.88	0.12	1575	100.0%	0.06 [0.05, 0.07]	2024
Total (95% CI)			**1685**			**1671**	**100.0%**	**0.06 [0.05, 0.07]**	

Heterogeneity: $Chi^2 = 10.32$, df = 1 (P = 0.001); $I^2 = 90\%$
Test for overall effect: Z = 14.13 (P < 0.00001)

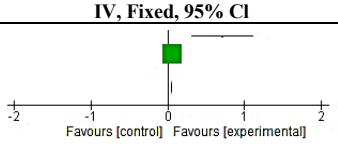

Figure 4. Forrest Plot of Changes in the Delayed Recall component of the MoCA score after follow-up

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Qiang Dong 2023	0.28	0.75	97	-0.11	0.75	96	0.1%	0.39 [0.18, 0.60]	2023
Xia Meng 2024	0.92	0.1	1588	0.91	0.1	1575	99.9%	0.01 [0.00, 0.02]	2024
Total (95% CI)			**1685**			**1671**	**100.0%**	**0.01 [0.00, 0.02]**	

Heterogeneity: $Chi^2 = 12.37$, df = 1 (P = 0.004); $I^2 = 92\%$
Test for overall effect: Z = 2.93 (P < 0.003)

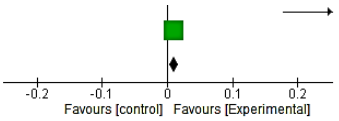

Figure 5. Forrest Plot of Changes in the Orientation component of the MoCA score after follow-up

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Qiang Dong 2023	0.45	1.05	97	0.09	1.08	96	0.0%	0.36 [0.06, 0.66]	2023
Xia Meng 2024	0.75	0.08	1588	0.68	0.08	1575	100.0%	0.07 [0.06, 0.08]	2024
Total (95% CI)			**1685**			**1671**	**100.0%**	**0.07 [0.06, 0.08]**	

Heterogeneity: $Chi^2 = 3.58$, df = 1 (P = 0.06); $I^2 = 72\%$
Test for overall effect: Z = 24.64 (P < 0.00001)

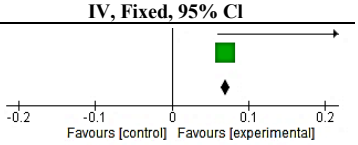

Figure 6. Forrest Plot of Changes in the Language component of the MoCA score after follow-up

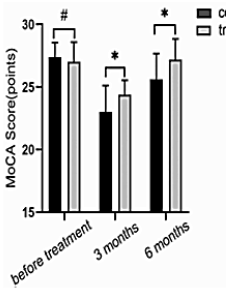

Figure 7. Comparison of the MoCA score between the two groups at pre-treatment, 3 months, and 6 months post-treatment. ($^{\#}P > 0.05$, $*P < 0.05$, using t-test)[9]

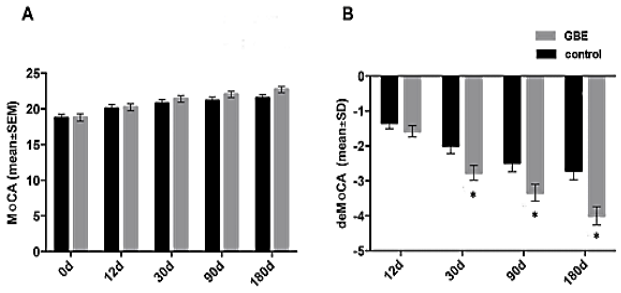

Figure 8. Comparison of the MoCA score between the two groups. (A) MoCA scores after acute stroke in the Ginkgo biloba extract (GBE) group and the control group at admission (B). Decline in MoCA scores (deMoCA) after acute stroke in the GBE and control groups. deMoCA, MoCA score at admission, and MoCA score at the indicated time points. *P<0.05 vs control[8]

Figure 3's plot summary shows a slight effect favoring the experimental group. Adding Ginkgo Biloba extract had a statistically significant impact on improving the MoCA score after follow-up, but with substantial heterogeneity. (MD = 0.47, 95% CI: [0.45-0.49], I^2 = 76%, and P<0.00001). Figures 4, 5, and 6 above are a forest plot of changes in three sub-domains of the MoCA, specifically scores for delayed recall, orientation, and language components. All of the plots suggests a small and statistically significant effect favoring the experimental group (MD = 0.06, 95% CI: [0.05-0.07], I^2 = 90%, and P<0.00001; MD = 0.01, 95% CI: [0.00-0.02], I^2 = 92%, and P=0.003; MD = 0.07, 95% CI: [0.06-0.08], I^2 = 92%, and P<0.00001, respectively) (Figure 4, Figure 5, and Figure 6).

We could not perform a statistical analysis on Liu et al in 2024 and Li et al in 2017 data, because it is the only articles that supplied data on the total MoCA score and deMoCA score, respectively (Figure 2). The decline in MoCA score (deMoCA) is often used in research to track cognitive changes over time, particularly in patients with conditions such as stroke or dementia, calculated by subtracting the MoCA score at a later time point from the initial baseline MoCA score.[9,16]

Liu et al.'s studies show statistically significant differences between the GDLM injection group and the control group (P > 0.05) at 3 and 6 months following therapy. However, they did not reach normal levels from baseline, with MoCA scores 24.46 ± 0.98 and 23.13 ± 1.43 at 3 months, and 27.22 ± 1.11 and 25.63 ± 1.25, respectively (Figure 7).

Li et al studies show statistically significant difference in deMoCA score, indicating GBE may promote MoCA score improvement, mainly at 30, 90, and 180 days (mean deMoCA in GBE group vs control group: −2.77±0.21 vs −1.99±0.23 at 30 days, P=0.0116; −3.34±0.24 vs −2.48±0.26 at 90 days, P=0.0165; −4.00±0.26 vs −2.71±0.26 at 180 days, P=0.0004) (Figure 8).[16]

Discussion

This systematic review evaluated the impact of adding Ginkgo biloba extract on cognitive function in patients with acute ischemic stroke. Two trials revealed substantial heterogeneity (I2 = 0.76), which may be due to the differences in the populations of the two studies. Xia Meng conducted trials involving patients aged 18-80, while Qiang Dong conducted studies only involving those aged 50 and above. Moreover, patients with any dementia or major neurological disorder like Parkinson's, Huntington's, Pick's, or Creutzfeldt-Jakob disease and seizure disorder were excluded from Qiang Dong's studies, while Xia Meng's studies were not. Another reason for substantial heterogeneity might be the different intervention types and follow-up lengths.[10,11] Although this systematic review reveals substantial heterogeneity, the addition of ginkgo biloba extract significantly impacts cognitive function, as indicated by the increase in MoCA score at the end of follow-up. (MD = 0.47, 95% CI: [0.45-0.49], I^2 = 76%, and P<0.00001). Sub-domain analysis reveals that ginkgo biloba extract has a significant impact on the delayed recall, orientation, and language components of the MoCA.[10,11]

The European Stroke Organization and European Academy of Neurology joint guidelines on post-stroke cognitive impairment have not recommended ginkgo biloba.[12] The consensus of the Asian Clinical Expert Group on Neurocognitive Disorders in 2019 recommended EGb as an essential part of the clinical treatment of neurodegenerative diseases.[13]

Ginkgo biloba extract is effective in various cerebrovascular diseases, but its treatment efficacy in CSVD has not been fully understood.[19] Ginkgo biloba extract has been used to prevent and treat stroke due to its potential to regulate neuroinflammation, decoy neuronal apoptosis, and reduce brain edema.[17-18] It has been proven to be beneficial to cognitive recovery.

Among all the main active ingredients, ginkgolide B exhibits the most vigorous activity in treating cerebrovascular disease by blocking inflammatory responses through participation in platelet-activating factor (PAF)-mediated signal transduction and attenuating neuronal damage by regulating the miR-206/BDNF signaling pathway.[14] Moreover, GB seems to play a positive role in differentiating neural stem cells after stroke by upregulating SOCS2 to activate the EGF receptor.[15] From another previous experimental study, ginkgo biloba extract has shown a positive therapeutic effect on CSVD rats, by reducing the concentration of inflammation markers (IL-18, TGF-β1, TNF-α, and Aβ1-40) and higher VEGF levels, which are specific to increasing vascular permeability, promoting extracellular matrix degeneration, vascular endothelial cell migration, proliferation, and angiogenesis [20,21]

This study has some limitations. First, all the study participants were Chinese, which could affect the generalization of the results. Second, inconsistent treatment methods in the control group and variations in drug dosage may affect the evaluation of the efficacy and safety of the intervention. Third, the author cannot determine which MoCA domain is more affected because it is not mentioned in the publication.

Conclusion

Adding Ginkgo biloba extract may improve the MoCA score in patients with acute ischemic stroke. Further research is needed to examine the effect on cognitive function using the MoCA score, with a specific domain or other criteria, or scoring methods to reduce bias.

References

1. Owolabi MO, Thrift AG, Mahal A, et al. Primary stroke prevention worldwide: translating evidence into action. Lancet Public Health; 2022. 7(1):e14. DOI: 10.1016/S2468-2667(21)00281-4
2. Huang YY, Chen SD, Leng XY, et al. Post-Stroke Cognitive Impairment: Epidemiology, Risk Factors, and Management. J Alzheimers Dis; 2022. 86(3):983-999. DOI: 10.3233/JAD-215644
3. Nys GM, van Zandvoort MJ, de Kort PL, et al. Restrictions of the Mini-Mental State Examination in acute stroke. Arch Clin Neuropsychol; 2015. 20:623-9. DOI: 10.1016/j.acn.2015.04.001
4. Haupt M, Gerner ST, Bähr M, Doeppner TR. Neuroprotective Strategies for Ischemic Stroke: Future Perspectives. Int J Mol Sci; 2023. 24(5):4334. DOI: 10.3390/ijms24054334
5. Dong Y, Li H, Dong Q. The effect of intravenous ginkgolide on clinical improvement of patients with acute ischemic stroke. Neurol Res; 2020. 42:260–266. DOI: 10.1080/01616412.2020.1724462
6. Wang TJ, Wu ZY, Yang CH, Cao L, Wang ZZ, Cao ZY, et al. Multiple mechanistic models reveal the neuroprotective effects of diterpene ginkgolides against astrocyte-mediated demyelination via the PAF-PAFR pathway. The American Journal of Chinese Medicine; 2022. 50(6):1565–1597. DOI: 10.1142/S0192415X22500665
7. Tomino C, Ilari S, Solfrizzi V, et al. Mild Cognitive Impairment and Mild Dementia: The Role of Ginkgo biloba (EGb 761®). Pharmaceuticals (Basel); 2021. 14(4):305. DOI: 10.3390/ph14040305
8. Li MZ, Zhang Y, Zou HY, Ouyang JY, Zhan Y, Yang L, et al. Investigation of Ginkgo biloba extract (EGb 761) promotes neurovascular restoration and axonal remodeling after embolic stroke in rats using magnetic resonance imaging and histopathological analysis. Biomed. Pharmacother; 2018. 103:989–1001. DOI: 10.1016/j. biopha.2018.04.125
9. Zhang M, Hu X, Wang T, & Liu X. Effectiveness of ginkgo diterpene lactone meglumine on cognitive function in patients with acute ischemic stroke. Open Medicine; 2024. 19(1):20240908. DOI: 10.1515/med-2024-0908
10. Cui M, You T, Zhao Y, Liu R, Guan Y, Liu J, et al. Ginkgo biloba extract EGb 761® improves cognition and overall condition after ischemic stroke: Results from a pilot randomized trial. Front. Pharmacol; 2023. 14:1147860. DOI: 10.3389/fphar.2023.1147860
11. Tian X, Xu Q, Xia X, Zhang Y, Meng X, & Wang A. Efficacy of ginkgo diterpene lactone meglumine on cognitive function in patients with acute ischemic stroke: a predefined exploratory analysis of a multicenter, double-blind, randomized controlled trial. Journal of Neurology; 2024. 271(6):3321–3327. DOI: 10.1007/s00415-024-12272-w
12. Quinn TJ, Richard E, Teuschl Y, Gattringer T, Hafdi M, O'Brien JT, Merriman N, et al. European Stroke Organisation and European Academy of Neurology joint guidelines on post-stroke cognitive impairment. Eur J Neurol; 2021. 28(12):3883-3920. DOI: 10.1111/ene.15068.
13. Zhan M, Sun L, Liu J, Zeng Z, Shen W, Li H, Wang, Y, et al. EGb in the Treatment for Patients with VCI: A Systematic Review and Meta-Analysis. Oxidative medicine and cellular longevity; 2021. DOI: 10.1155/2021/8787684
14. Li Y, Zhang M, Li S, Zhang L, Kim J, Qiu Q, et al. Selective ischemic-hemisphere targeting Ginkgolide B liposomes with improved solubility and therapeutic efficacy for cerebral ischemia-reperfusion injury. Asian journal of pharmaceutical sciences; 2023. 18(2):100783. DOI: 10.1016/j.ajps.2023.100783
15. Zheng PD, Mungur R, Zhou HJ, Hassan M, Jiang SN, Zheng JS. Ginkgolide B promotes the proliferation and

differentiation of neural stem cells following cerebral ischemia/reperfusion injury, both in vivo and in vitro. Neural Regeneration Research; 2018. 13(7):1204-11. DOI: 10.4103/1673-5374.232476

16. Li S, Zhang X, Fang Q, Zhou J, Zhang M, Wang H, et al. Ginkgo biloba extract improved cognitive and neurological functions of acute ischaemic stroke: A randomised controlled trial. Stroke and Vascular Neurology; 2017. 2(4):189–197. DOI: 10.1136/svn-2017-000104
17. Cui M, You T, Zhao Y, Liu R, Guan Y, Liu J, et al. Ginkgo biloba extract EGb 761® improves cognition and overall condition after ischemic stroke: Results from a pilot randomized trial. Front Pharmacol; 2023. 14:1147860. DOI: 10.3389/fphar.2023.1147860.
18. Jiang S, Ma X, Chen Y, Gu B, Sun N, Xiao H. Effects of ginkgo diterpene lactone on brain inflammation and oxidative stress in rats with cognitive impairment of cerebral small vessel disease. Am J Transl Res; 2021. 13(6):6382–90.
19. Geng JL, Aa JY, Feng SQ, Wang SY, Wang P, Zhang Y, et al. Exploring the neuroprotective effects of ginkgolides injection in a rodent model of cerebral ischemia-reperfusion injury by GC-MS based metabolomic profiling. J Pharm Biomed Anal; 2017. 142:190–200. DOI: 10.1016/j.jpba.2017.04.031
20. Karaman S, Leppanen VM, Alitalo K. Vascular endothelial growth factor signaling in development and disease. Development; 2018. 145:dev151019. DOI: 10.1242/dev.151019
21. Tabrez S. Editorial: cures of vascular disease - the state. Curr Vasc Pharmacol; 2017. 15:290. DOI: 10.2174/1570161115041706141532 46