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RESEARCH ARTICLE

The effect of *Ginkgo biloba* on the liver, brain and heart of induced ischemic stroke rats

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ABSTRACT

Background: A stroke is a medical condition in which poor blood flow to the brain may result in death. Death as an outcome of stroke is not always the case as partial disabilities and paralysis may happen as well. The use of animal models in recent years has provided a better understanding of the pathophysiologic mechanisms of stroke. **Aim:** The present study aims to examine the effect of *Ginkgo biloba* on induced ischemic stroke in rats. **Material and Methods:** This study was conducted on 60 adult rats weighing 180 ± 20 gm and of 10-12 weeks in age. *Ginkgo biloba,* the dietary supplement was given orally in ischemic-stroke-induced rats. Hematological and biochemical serum analysis, as well as histological examination, were done to explore the ameliorative effect of ginkgo extract. **Results:** ANOVA results showed a statistically significant difference in hemoglobin, hematocrit, platelet count, urea, cholesterol, triglycerides, glucose, FT3 and TSH. *Post-hoc* analysis showed significant increases in urea, cholesterol, triglycerides, glucose, and TSH, while a decrease in platelet count in the ischemic-stroke-induced rats compared with the controls. On the other hand, the group that received *G. biloba* showed significant decreases in urea, glucose, FT3 and TSH, while the platelet counts significantly increased compared with the ischemic-stroke-induced rats. In comparison between the control group with the group that was given *G. biloba,* a significant increase in triglycerides was noticed. Histology examination demonstrated several alterations in brain, heart and thyroird in ischemic-stroke-induced rats that have been recovered after *G. biloba* treatment. However, *G. biloba* induced negative alterations in the thyroid. **Conclusion:** The results obtained in this study demonstrated that *G. biloba*-treated group showed better biomarkers. However, *G. biloba* had unwanted effects on triglycerides and thyroid as observed. Further study on the effect of *G. biloba* on the thyroid gland is required.

Keywords: Brain stroke, environment, *Gingko biloba*

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INTRODUCTION

A stroke is considered a medical condition during which poor blood flow to the brain leads to death. If symptoms last for two hours, it is referred to as a transient ischemic attack (TIA) or mini-stroke. When blood is partly provided to the brain, this results in the pathology of the brain tissue in this space. There are four reasons why this occlusion or embolism would possibly happen (Donnan et al., 2008). There are two main kinds of hemorrhage (Goldstein and Simel, 2005). Neural structure hemorrhage, is largely injury within the brain itself, flooding the encompassing tissue with blood because of either intra-parenchymal hemorrhage or cavum hemorrhage. Animals have been used as a model to study a stroke (Fluri et al., 2015)

The relevance of results obtained from animals to the treatment of human diseases has been restricted, as occurred with neuroprotection. Neuroprotection is an intervention, typically involving drug administration that acts directly on the intracellular mechanisms of the anemia cascade to affect the stroke (Teocchi, 2010). Speedy identification of symptoms allows for improved treatment choices and outcomes.

Another distinction between animal models and humans is the rigorous management of the animals used (Wessmann et al., 2009). Several intergroup variations emerged as well as the overall volume of affected tissue, swelling formation, and purposeful consequences (Joutel, 2010). Mice were the foremost unremarkably used animal model. Careful anatomic information about the encephalic vessels of assorted species is important for developing a reliable and helpful model of the pathology (Fagundes and Taha, 2004). The use of various models is beneficial for experimental studies on anemia, preventing the event of a customary surgical model. The best model has the characteristics of clinical relevancy, simple experimental execution, and reliability. Many strategies of anemia induction are represented. Variation in time of anemia contributes to the variety of the experimental models used; the foremost used technique for inducement anemia is occlusion by middle artery occlusion (Calloni, 2006). In tests of motor behavior, animals are given different degrees of useful defects on the contralateral aspect of the anemia. Histologically, middle artery occlusion produces tiny death in central and apoptotic peripheral regions (Mendez-Otero et al., 2009).

Over the previous decades, the maidenhair tree leaf extract has stepped into the seasoning spotlight principally attributable to its established edges for treating presenile dementia (Yao et al., 2004). It conjointly seems promising as a therapeutic for several different chronic and acute sorts of diseases (Izzo and Ernst, 2001). The bioavailability of flavonoids is comparatively low because of restricted absorption and fast elimination. Flavonoids within the glycosidic type are poorly absorbed within the intestine; solely within the aglycone type, they are absorbed directly (Goh and Barlow, 2004). Unabsorbed flavonoids that reach the colon are also subject to metabolism by microorganism enzymes, and so absorbed (DeFeudis and Drieu, 2000). Once absorbed, flavonoids reach the liver wherever they are metabolized to conjugate derivatives. It is well-known that the biological activities of flavonoid metabolites do not seem to be continuously equivalent to those of the parent compound (Manach et al., 2004). Two sorts of terpenoids are gift in gingko as lactones (nonsaponifiable lipids gifted as cyclic esters): ginkgolides and also bilobalide (Smith and Lou, 2004). Ginkgolides are diterpenes with five varieties A, B, C, J, and M; where A, B, and C account for around three. One per cent of the whole gingko leaf extract (DeFeudis and Drieu, 2000). Bilobalide, a sesquiterpene trilactone, accounts for the remaining 9% of the whole standardized ginkgo leaf extract (Smith and Luo, 2004). The counseled dose of standardized extract, EGb 761, is 40-60 mg, three times daily in supported clinical trials (Mahady, 2001). For chronic conditions, the German commission recommends a minimum 8-wk intake to watch the helpful effects of the ginkgo leaf extract (McKenna et al., 2001). Hence, this work aimed to experimentally study the effect of *Ginkgo biloba* on induced ischemic stroke in rats. For that, we examined the changes in the biochemical serum analysis including thyroid hormones and tissue histology.

MATERIAL AND METHODS

Animal husbandry

This study was conducted on 60 adult rats weighing (180 ± 200 gm) with the age range of (10-12) weeks (Animal facility of the High Institute of Public Health, Alexandria University, Alexandria, Egypt). The animals were housed in wire mesh cages, at room temperature 22-24 °C and 12h: 12h light/dark cycle. They were fed a standard diet (20% casein, 15% corn oil, 55% corn starch, 5% salt mixture and 5% vitaminized starch (Egyptian Company of Oils and Soap, Kafr-Elzayat, Egypt) and allowed water by *ad libitum*. The dietary supplement used (*G. biloba)* was purchased from EMA Pharma pharmaceutical (Cairo, Egypt).

experimental setup

The experimental animals were divided into four groups (15 rats each). Group I (control normal rats): eight rats (35.3%) were females and seven rats (46.7%) were males. Group II (rats with stroke): seven rats (46.7%) were females and the other eight rats (53.3%) were males, stimulating the ischemic stroke to rats by intraluminal filament method (Ahmad et al., 2012). Group III (rats with stroke treated with *G. biloba* in doses 100 g/kg, 9 times orally): eight rats (53.3%) were females and the other seven

(46.7%) were males. Group IV (normal rats given *G. biloba* without causing the stroke): seven rats (46.7%) were females and the other eight (53.3%) were males. Rats were administrated *G. biloba* (100 mg/Kg body weight) 9 times oral gavage day after day according to Rodriguez de Turco et al. (1983). This work has been done following the Ethical approval in Alexandria University Faculty of Medicine under No. 0105356.

Preparation of rats to stimulate the ischemic stroke by intraluminal filament method: The rats fasted along the night, and prior to the treatment, they were anesthetized intravenously with 10 mg ketamine through vena caudles. The middle cerebral artery was bound with slight modification (Ahmad et al. 2012). Operation space was cleaned up using a scissor, and the skin around the petrosum of scapula was incised and the neck muscle was displaced to reach the common carotid artery. Dissection was done on bifurcation carotid artery and carotid glomus around nervus vagus. The occipital artery, the branch of the external carotid artery was carefully displaced from blood glucose, lipid profile and serum thyroid hormones. For the determination of blood parameters, blood samples were collected into EDTA–treated tubes. The hematological parameters determined were RBCs count, Hemoglobin (Hb) content, Haematocrit value, Platelet (Plt) count and total Leucocytes count. In the same experiment, tissue of the brain, thyroid gland and heart were collected and divided into small parts to conduct a histological investigation.

Hematological and Biochemical analyses

Determination of the RBCs, total leucocyte and platelet count was done according to Wintrobe (1976), Miale (1972) and Seiverd (1983), respectively. Determination of haemoglobin content was done according to Dacie and Lewis (1975). Determination of Haematocrit value was performed according to Oser ((1979. Determination of serum blood sugar, total cholesterol, triglycerides and Uric acid was done according to Young et al. (1972), Allain et al. (1974) and Fossati and Prencipe (1982), respectively. Determination of alanine aminotransferase and aspartate transaminase carotid artery. The internal carotid artery was carefully displaced on the distal part, an entrance into intracranial. The internal carotid artery was then branched into pterigo palatinum nearby proximal, an entrance into the head. The location of the middle cerebral artery is about 17-20 mm from the bifurcation common carotid artery. After all the arteries have been identified, then occlusion was done by binding the common carotid artery, external carotid artery, and internal carotid artery on the proximal of a middle cerebral artery. Occlusion was done for 2 h, and then the binding was released for reperfusion for 7 days. Treatment of Wistar rats with medicine or antioxidants can be done after reperfusion (Ahmad et al. 2012).

Sample collection

At the end of the experiment period, rats were dissected and blood samples were individually collected according to Paradopoulos et al. (2010), then centrifuged at 3000 x g for 15 minutes to obtain serum. Serum was stored at -80 °C freezer until use. the biomedical analyses estimated were kidney function, liver function,

activity was according to Kachmar and Moss (1976). Determination of urea and Creatinine concentrations in serum was done according to the method of Patton and Crouch (1977) and Bowers and Wong (1980), respectively. Determination of Free T3 and T4 concentration according to Maes (1997) and Thakur et al. (1997), respectively. Determination of Thyroid Stimulating Hormone concentration according to Morimoto and Santoro (1998).

Histological investigation

Brain, thyroid gland and heart were immediately removed from the dissected rats, divided into small pieces and immediately fixed by immersion in 10% buffered formalin solution then left for 24–48 h. The specimens were then dehydrated, cleared and embedded in paraffin. Serial sections of 5 µm thick were cut using the rotary microtome and stained with Haematoxylin and Eosin (H&E) (Bancroft et al., 1994). All sections were examined under light microscopy equipped with a digital camera for photo capture.

Statistical analysis

Data were expressed as Mean ± standard deviation. Normality was checked, and then the difference among means was tested using one-way ANOVA, followed by Tukey multiple comparisons between groups. The statistical difference was considered significant at $P<0.05$.

RESULTS AND DISCUSSION

Leukocytes are the first cells that arrive in the stroke region(s), and they increase in peripheral blood. Leukocytosis on admission was related to initial stroke severity but not to the outcome. Leukocyte count on admission seems merely to reflect initial stroke severity and is most likely a stress response with no independent influence on the outcome (Kazmierski et al., 2001). The persistence of leukocytosis can ultimately lead to worse neurologic outcomes. Leukocyte migration and accumulation were measured using leukocytes labeled with radioactive markers and scintigraphy or single-photon emission computed tomography. The present study, along with several others, has evaluated the efficacy of using WBC count as a prognostic marker among patients with acute ischemic stroke. However, we did not find statistical differences among the groups in RBC and WBC counts (Table 1). Hematological parameters are used for the diagnosis and prognosis of several hematological diseases (Nadkarn et al., 2009). Hematological analyses are found to be useful for prognosis and can be of immense value for stroke patients; like erythrocyte sedimentation rate (ESR), platelet count and leukocyte count in blood samples collected at the time of admission for prediction of stroke outcome (Yoon and Zheng, 2005). In the present study, there is no significant differences were found between the ischemic stroke group and the control in hematocrit and haemoglobin (Table 1). Researchers found that anemia was present in about a quarter of patients with stroke upon admission and was associated with a higher risk of death for up to one year following either ischemic stroke or hemorrhagic stroke.

Circulating platelets play a critical role in the development of ischemic stroke by acting as a mediator for other circulating cells by facilitating activation (Thomas and Storey 2015). Du et al. (2016) found a positive correlation between elevated platelet count (PC) and the risk of stroke recurrence. Some studies indicated that PC was significantly lower in patients with ischemic stroke and myocardial infarction compared with healthy controls (Ranjith et al*.,* 2009). Similarly, we observed lower PC in the ischemic rats than in the controls (Table 1). However, other studies presented a positive correlation between PC level and platelet-induced pro-thrombotic (Li et al. 2016). It is possible to speculate that the two mechanisms, platelet consumption and platelet-induced inflammation, reached lower activity at intermediate PC, making platelet count of a prognostic significance for improved risk stratification of adverse clinical outcomes in ischemic stroke and TIA patients (Elkind et al., 2014). Two hours after brain ischemia/ reperfusion in rats with a fatty diet, a sharp decline in the activity of antioxidant enzymes and increased levels of malondialdehyde and free calcium in the liver were observed (Parikh et al*.,* 2017). However, Abdeldyem et al. (2017) showed that the initiation of inflammatory response was detected only on the 5th day of the experiment.

The association of kidney dysfunction (an increase of urea) with post-stroke outcomes may be because of several possible factors. Renal impairment in patients with stroke may indicate end-organ damage from common risk factors, such as uncontrolled hypertension or other comorbidities (MacWalter et al., 2002). Renal impairment may cause endothelial dysfunction, homocystenemia, coagulation disorders, and extravascular coagulation (El Husseini et al*.,* 2014). The present results showed a statistically significant increase in urea after ischemic stroke (Figure 1). The present findings further extend and strengthen previous studies suggesting that renal dysfunction may be associated with increased post-stroke mortality (Putaala et al., 2011). MacWalter et al. (2002) reported that high serum urea concentrations post-stroke was associated with a higher risk of all-cause mortality. It is difficult to establish an independent relation of hyperuricemia with ischemic stroke. Some studies revealed hyperuricemia as a protective factor of ischemic stroke (Chamorro et al., 2004).

Table 1. Comparison between different studied groups regarding rat's blood cells test

Blood picture	Group I (Control) n=15	Group II (Rats with stroke) n=15	Group III (Stroke rats treated with G.B) n=15	Group IV (Normal rats given G.B) n=15
WBCs(thousands/cmm)				
Range	2.4-7.7	2.99-8.1	2.6-6.9	3.85-6.33
Mean	5.05	5.28	4.88	5.18
S.D.	1.47	1.58	1.28	0.73
ANOVA	0.262			
P value	0.852			
P1		0.631	0.721	0.794
P2			0.403	0.826
P3				0.537
RBCs (millions/cmm)				
Range	6.55-9.44	7.27-9.65	6.22-9.67	6.12-9.22
Mean	8.35	8.53	8.12	8.10
S.D.	0.90	0.67	1.00	0.83
ANOVA	0.847			
P value	0.474			
P1		0.582	0.463	0.417
P2			0.201	0.176
P3				0.937
Hb(g/dl)				
Range	11-16	13.7-18.3	11.5-18	12.4-18.2
Mean	14.29	15.27	15.48	16.32
S.D.	1.57	1.44	1.60	1.65
ANOVA	4.268			
P value	0.009 *			
P1		0.090	0.041*	0.001**
P2			0.719	0.073
P3				0.147
Hct (%)	34-52	39-52.5	39.1-51	40.3-52
Range	45.53	43.42	43.99	48.33
Mean	5.66	4.02	3.09	3.35
S.D.				
ANOVA	4.207			
P value	0.009*			
P1		0.169	0.314	0.070
P2			0.707	0.002*
P3				0.006 *
Plt(thousands/cm)				
Range	699-1100	1266-1630	730-1200	799-1001
Mean	892.33	1390.07	1045.80	927.27
S.D.	114.64	94.56	126.02	61.41
ANOVA	74.189			
P value	0.001**			
P1		0.001**	0.001**	0.353
P2			0.001**	0.001**
P3				0.002*

P1 comparison between the control group and other groups, P2 comparison between group II and both group III and IV, P3 comparison between group III and IV, N.S. not significant, * Significant at level 0.05, **Highly significant at level 0.001.

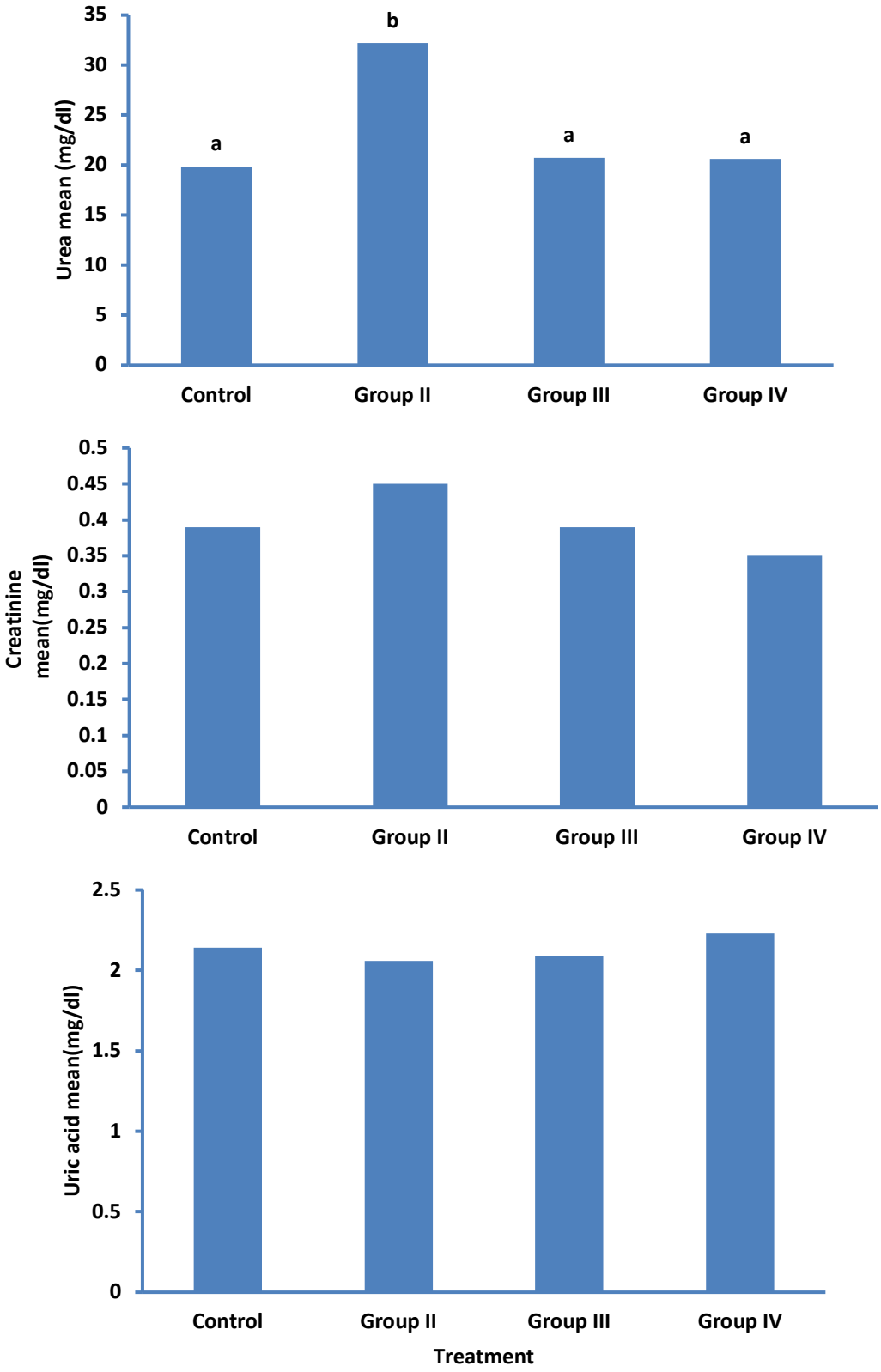

Figure 1. Comparison between different studied groups regarding kidney function. Group I: control rats, Group II: rats with stroke, Group III: rats with stroke treated with *Ginkgo biloba,* Group IV: normal rats given *G. biloba* without causing a stroke. *n* = 15. There is only a significant difference among the groups (one-way ANOVA) in urea. The bars with the same letter are not significantly different (Tukey test).

The present study showed that there are no significant differences among groups tested in the liver enzymes SGPT nor SGOT while there is a significant increase in cholesterol, triglycerides and glucose of ischemic-stroke rates compared with the control (Figures 2-4), which was probably influenced by inflammation. These results were inconsistent with Costa et al. (2011) who found that GOT/AST is the only liver enzyme directly associated with the ischemic cerebral lesion independently from inflammation. Possibly this enzyme, neutralizing the toxic glutamate, might play a protective role, as some reports on its favorable prognostic significance suggest (Sobrino et al., 2011). Associations between high serum total cholesterol (TC) levels and an increased risk of ischemic stroke have been reported. Most brain cholesterol originates from local synthesis rather than plasma lipoproteins and serum cholesterol does not necessarily correlate with its content in the CNS, it should be kept in mind that cholesterol is the essential constituent of plasma membranes, and regulates their fluidity and permeability (Murphy and Johnson, 2008). High triglycerides are associated with several abnormalities of the body's clotting systems, which may contribute further to their association with cardiovascular disease (Tanne et al., 2001). The current study showed that there is a statistically higher triglyceride level in the ischemic stroke rats compared with the controls. Bowman et al. (2003) also found that ischemic stroke patients had higher triglycerides than the controls. By provoking anaerobic metabolism, lactic acidosis, and free radical production, hyperglycemia may exert direct membrane lipid peroxidation and cell lysis in metabolically challenged tissues (Kernan et al. 2002).

Hypothyroidism can cause hypertension, hypercholesterolemia, cardiac dysfunction, and both hypo- and hypercoagulability, all of which are risk factors for stroke (Bai et al., 2014). Hyperthyroidism is also associated with atrial fibrillation, which is a common cause of cardioembolic stroke (Chen et al., 2014). Elevated concentrations of thyroid hormone (TSH) are associated with an increase in energy and oxygen demand, which would be expected to impair ischemic tolerance in the brain. The current study showed that THS was higher in ischemic rats than those in the controls, whereas no significant changes were observed in F3 or F4 (Figure 5). Wang et al. (2017) reported that the subgroup analysis indicated that in the acute phase of ischemic stroke, higher TSH was associated with better Fatigue Severity Scale scores in patients. However, more studies are required to determine the impact of thyroid function on cerebral ischemia (López et al*.,* 2010). Tri-iodothyronine (T3) can induce hypothermia, and anti-inflammation (Li et al., 2017).

Ginkgo biloba has a hepatic protective action on the liver and anti-oxidant defense properties. The leaf extract of *G. biloba* consists mainly of terpenoids and glycosides that have antioxidant potency (Raafat et al., 2013). It has been shown that *G. biloba* was able to rescue the cardiac phenotype in streptozotocin-induced diabetic rats (Li et al., 2017). In the present study, *G. biloba* caused a significant reduction in urea, glucose, F3 and TSH levels after giving *G. biloba* to ischemic stroke rats (Figures 1,4,5). After inducing ischemic stroke and being treated with *G. biloba* for 3 months, this demonstrated the importance of using *G. biloba* in reducing the level of serum urea. The flavonoids present in *G. biloba* may be responsible for its antioxidant as well as hypolipidemic action. Dubey et al. (2005) reported that treatment with GBE did not affect triglycerides, which was consistent with present results, that did not find any significant difference between the ischemic-stroke rats and those treated with *G. biloba* later (Figure 3). Previous studies showed that *G. biloba* extract effectively decreased fasting serum glucose levels, protected islet β-cell functions, and improved metabolic homeostasis in experimental animal models (Rhee et al*.,* 2015).

Kidney sections of diabetic rats showed an increase in mesangial cells and matrix of glomeruli with an increase in glycogen deposition and hyalinization of arteries with thickened basement membranes of proximal and distal convoluted tubules. These changes lead to a reduction in the glomeruli (Elghazaly et al., 2019b). The diabetic rats showed tubular casts, inflammatory cellular infiltration and glomerular atrophy (Elghazaly et al., 2019b).

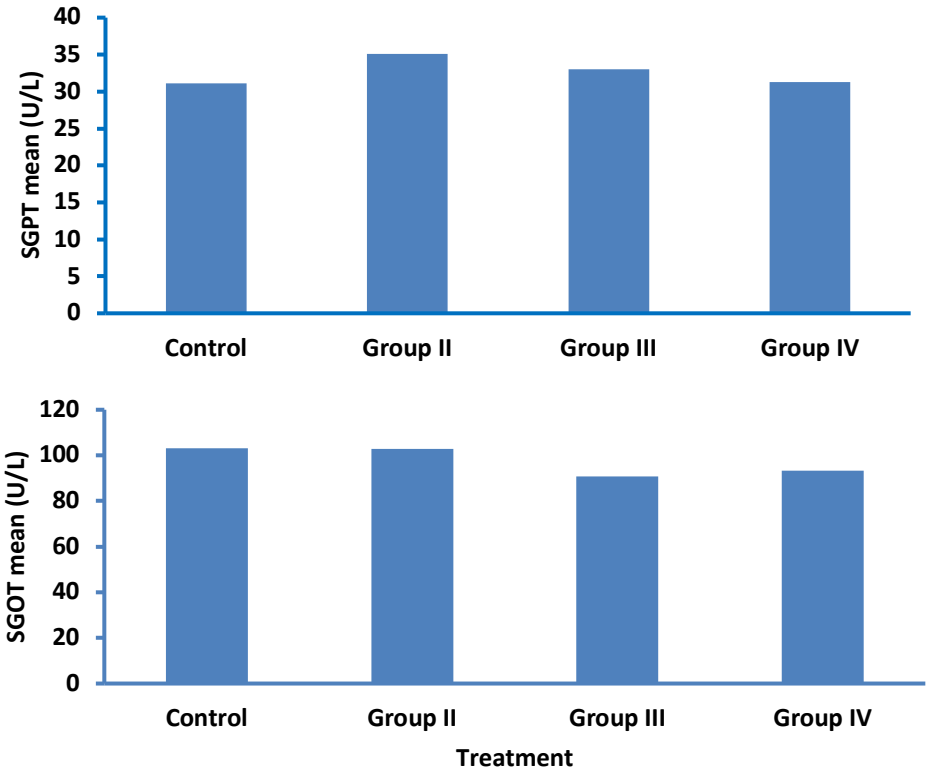

Fig. 2: Comparison between different studied groups regarding liver function. Group I: control rats, Group II: rats with stroke, Group III: rats with stroke treated with *Ginkgo biloba,* Group IV: normal rats given *G. biloba* without causing a stroke. *n* = 15. There is no significant difference among the groups (one-way ANOVA) in SGPT or SGOT.

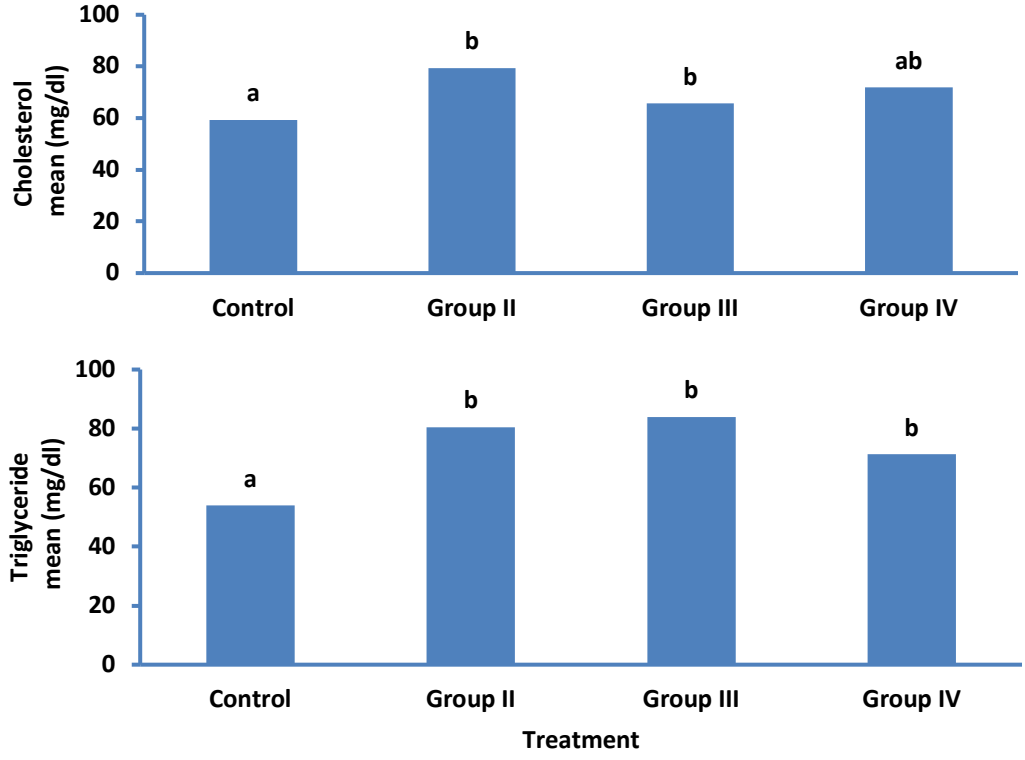

Figure 3. Comparison between different studied groups regarding lipid profile. Group I: control rats, Group II: rats with stroke, Group III: rats with stroke treated with *Ginkgo biloba,* Group IV: normal rats given *G. biloba* without causing a stroke. *n* = 15. There are significant differences among the groups (one-way ANOVA) in cholesterol and triglycerides. The bars with the same letter are not significantly different (Tukey test).

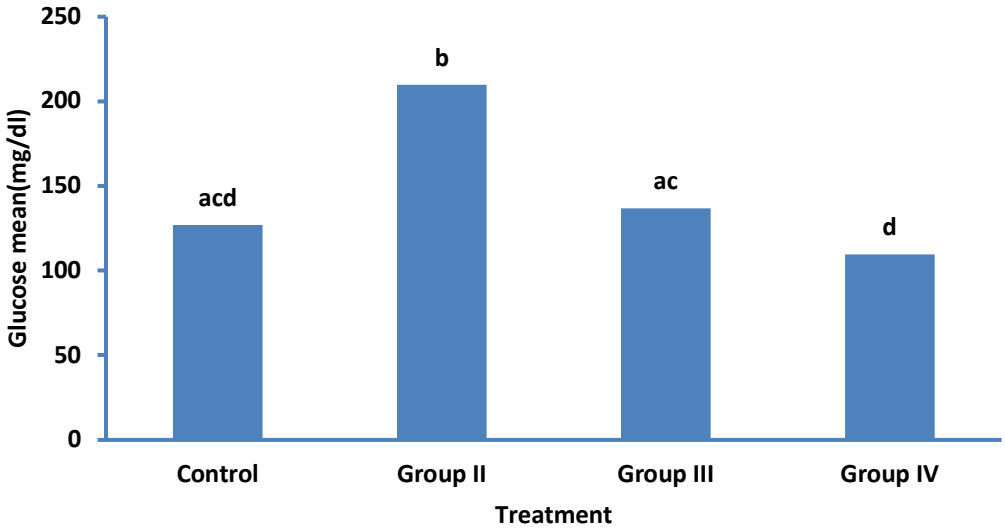

Figure 4. Comparison between different studied groups regarding Glucose. Group I: control rats, Group II: rats with stroke, Group III: rats with stroke treated with *Ginkgo biloba,* Group IV: normal rats given *G. biloba* without causing a stroke. *n* = 15. There is a significant difference among the groups (one-way ANOVA). The bars with the same letter are not significantly different (Tukey test).

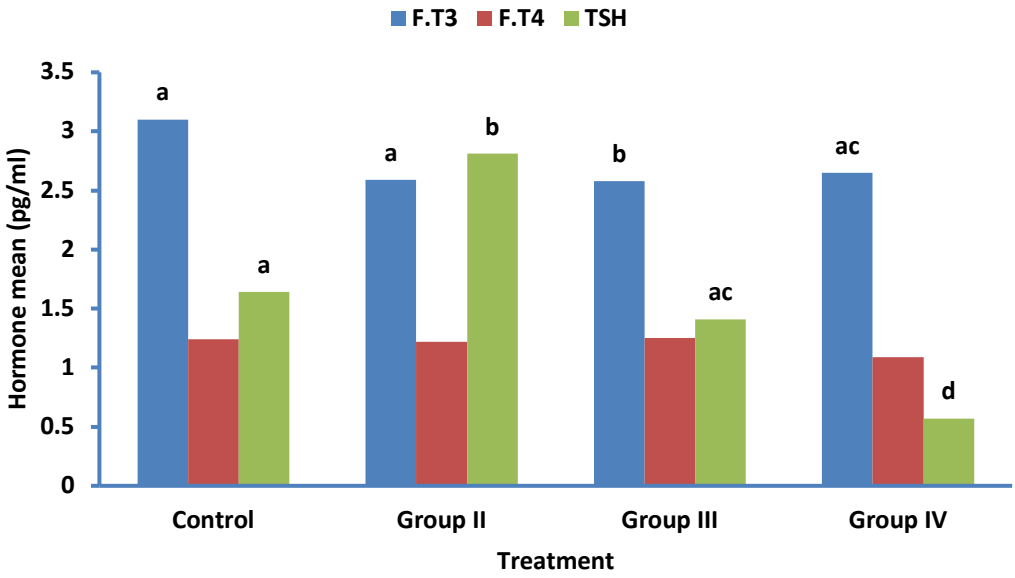

Figure 5. Comparison between different studied groups regarding thyroid hormones. Group I: control rats, Group II: rats with stroke, Group III: rats with stroke treated with *Ginkgo biloba,* Group IV: normal rats given *G. biloba* without causing a stroke. *n* = 15. There are significant differences among the groups (one-way ANOVA) in T4 and TSH. The bars with the same letter are not significantly different (Tukey test) within the same hormone.

The rats which were fed a high-fat diet for two weeks showed a larger number of inflammatory cells, degeneration of muscle fiber of the heart, circular and congested blood vessels (Elghazaly et al., 2019a). However, it was evident that treated normal rats with *G. biloba* exhibited higher haemoglobin and triglycerides and lower TSH (Table 1; Figures 3,5). These effects could suggest *G. biloba* may have some unwanted side effects on normal rats. In histology, the brain in Figure 6a shows a normal histological structure in the control. Group II (stroke rats) (6b) shows neurons appear pyramidal in shape and directed towards the cortex and congested blood vessels. After treatment with *G. biloba*, (6c-d) show areas of gliosis, increased space around some, and shrunken pyramidal cells, which appear with dark basophilic cytoplasm.

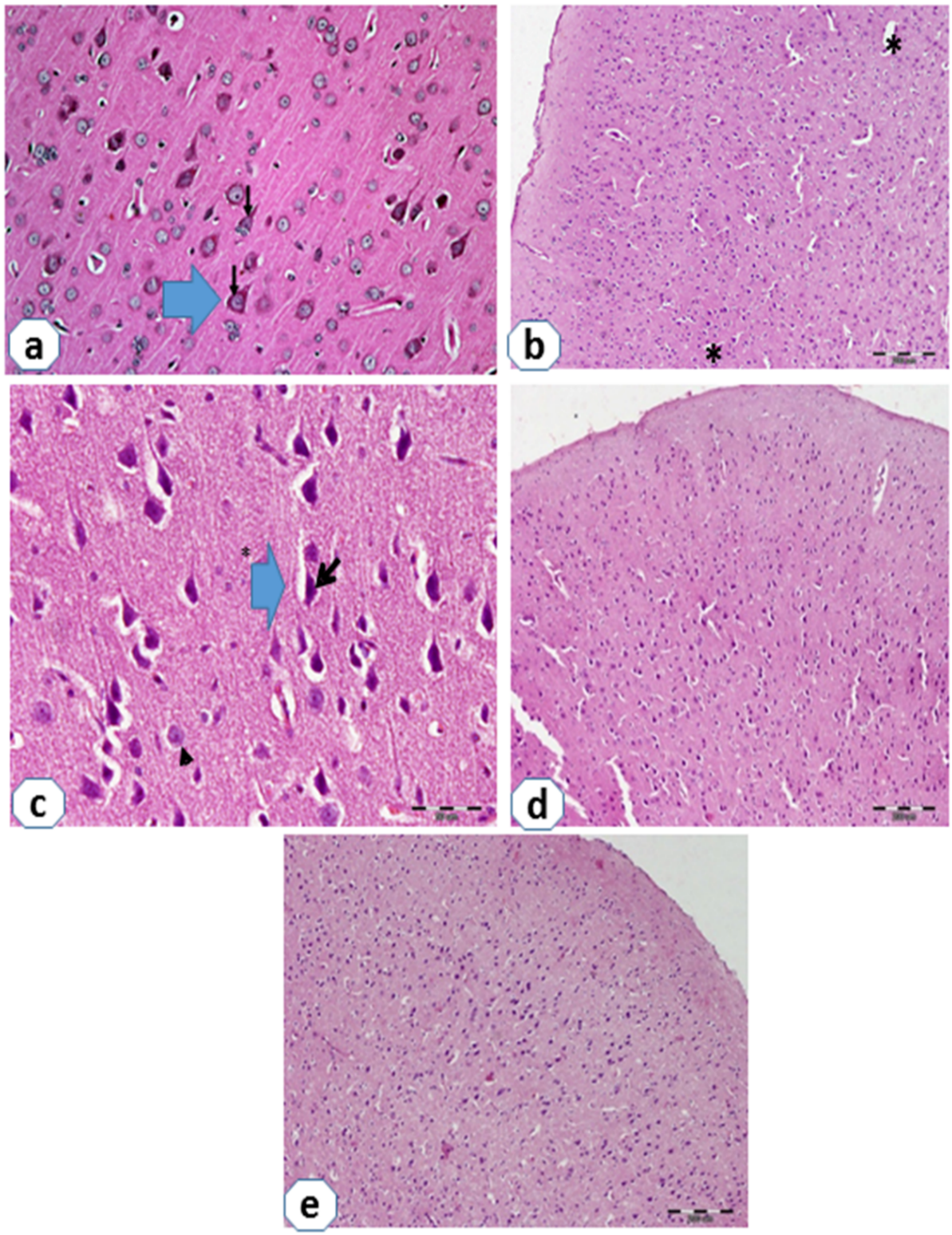

Figure 6. Photomicrograph of the cerebral cortex. Group I (control) show normal histological structure of brain tissue, different size and shape of pyramidal cells and nerve fibers were observed (↓) (a). Group II (stroke rats) shows neurons appear pyramidal in shape and directed towards the cortex, and congested blood vessels (*) (b). Group III (stroke rats treated with *Ginkgo biloba*) (c, d) shows areas of gliosis, increased space around some, and shrunken pyramidal cells, which appear with dark basophilic cytoplasm. Group IV (normal rats given *Ginkgo biloba)* (e) shows normal histological structure of brain tissue.

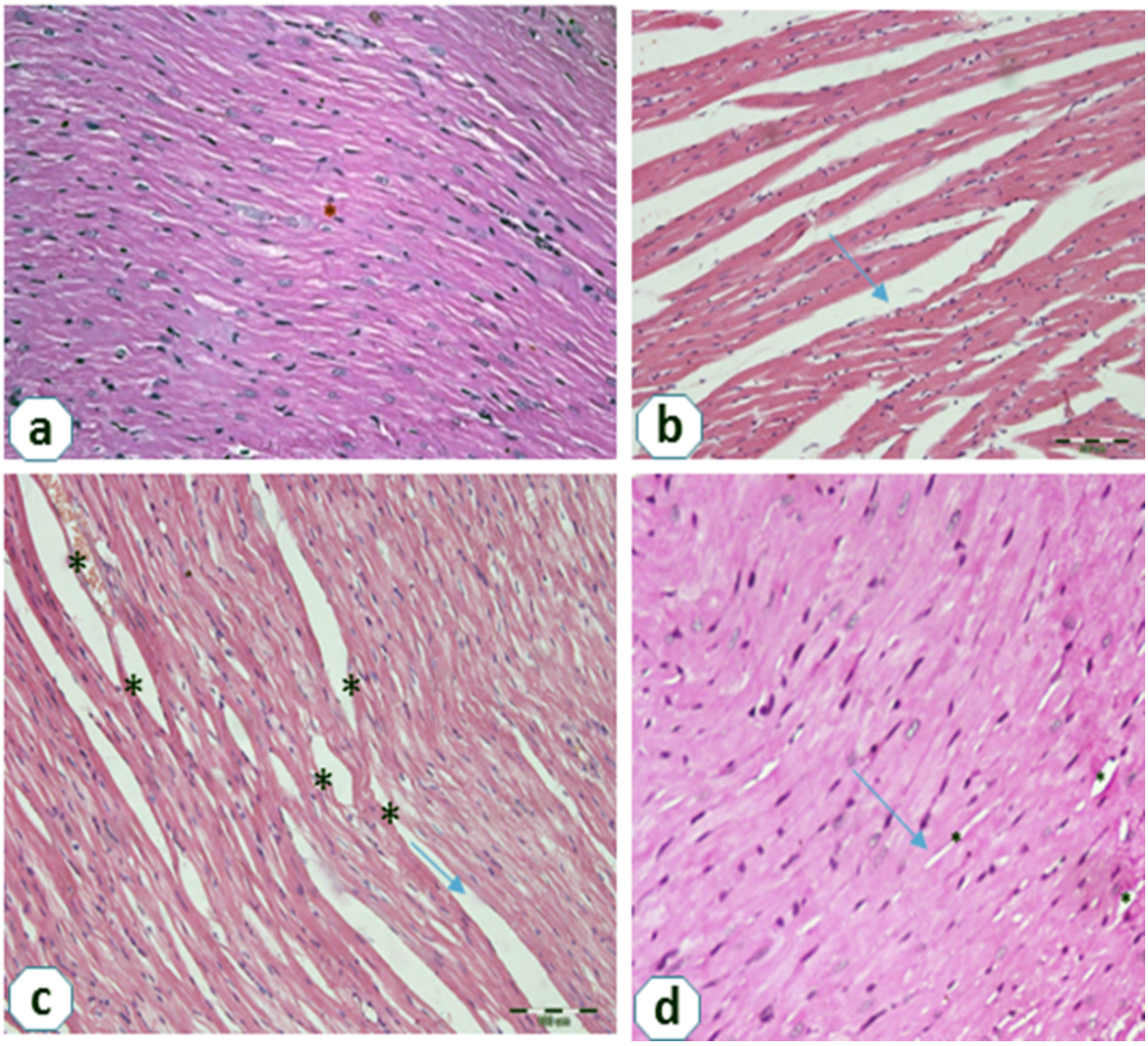

Figure 7. Photomicrograph of sections in the ventricular wall of cardiac muscle. Group I (control normal rats) show normal histological architecture of cardiac myocytes. Cylindrical branching of cardiac myocytes is with an acidophilic sarcoplasm and single oval nuclei; capillaries are found in the connective tissue between cardiac myocytes (*) (a). Group II (stroke rats) shows disrupted widely separated cardiac muscle fibers resulting in edema between myo-fibers (→) (b). Group III (stroke rats treated with *Ginkgo biloba*) shows wavy separated myofibrils with congested blood vessels (*) (c). Group IV (normal rats given *G. biloba*) shows normal histological architecture of cardiac myocytes; cylindrical branching of cardiac myocytes is with an acidophilic sarcoplasm and single oval nuclei. Capillaries are found in the connective tissue between cardiac myocytes (*) (d).

Brain of the rat

In the heart, (Figure 7) the control normal rats show a normal histological architecture of cardiac myocytes (a), while, stroke rats show disrupted widely separated cardiac muscle fibers resulting in edema between myo-fibers (b). However, stroke rats treated with *G. biloba* show wavy separated myofibrils with congested blood vessels (c).

Heart of the Rats

Figure 8 shows the thyroid in the adult albino rat (control group) with normal thyroid follicles lined with a single layer of epithelial cells (a); Group II (stroke rats) have irregular thyroid follicles lined with an organized single layer of epithelial cells; wide inter-follicular space is detected (b). Group III (stroke + *G. biloba*) shows Thyroid follicles of varying sizes. Some follicles lack colloid secretion. Some follicular cells were detected in lumen space. Cellular infiltration was detected (c & d). The normal rats given *G. biloba* show Thyroid follicles of varying sizes and follicles lacking colloid secretion.

Thyroid of Rats

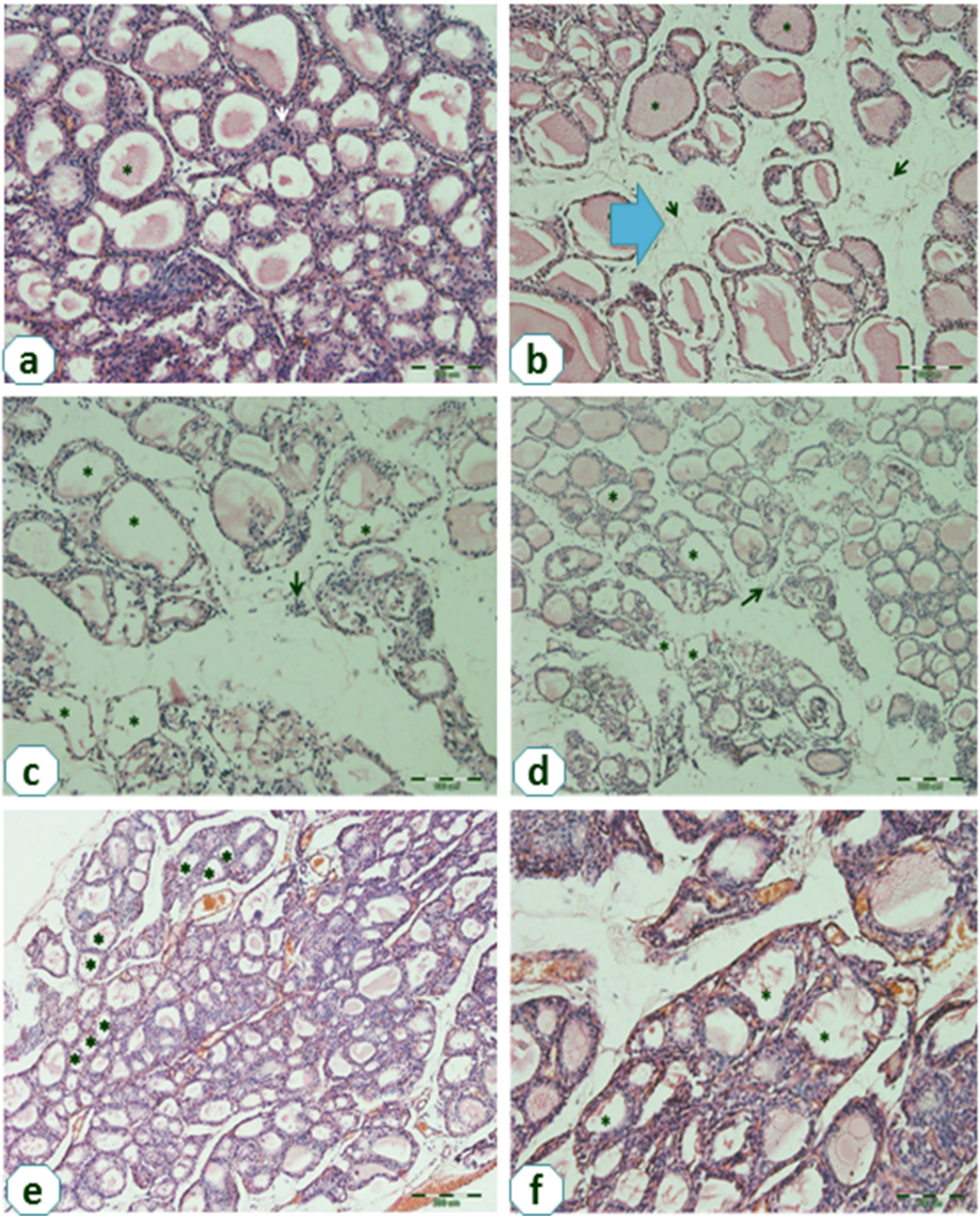

Figure 8. Photomicrograph of sections in the thyroid of the adult albino rat. Group I (control) show normal thyroid follicles lined with a single layer of epithelial cells. The follicles are filled with homogeneous colloids. There are many inter-follicular tissues (a). Group II (stroke rats) shows irregular thyroid follicles lined with an organized single layer of epithelial cells; The follicles are filled with colloid (*); There is no inter-follicular tissue; wide inter-follicular space is detected (b). Group III (stroke + *Ginkgo biloba*) shows thyroid follicles of varying sizes. Some follicles lack colloid secretion (*). Some follicular cells were detected in the lumen space. Cellular infiltration was detected (c & d). Group IV (normal rats given *G. biloba*) shows thyroid follicles of varying size (many follicles are small and not organized; follicles lack colloid secretion (*), absent of inter-follicular tissue, congested dilated blood vessels and marked cellular infiltration (e & f).

CONFLICT OF INTEREST

No conflict of interest.

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AVAILABILITY OF DATA

The datasets in the current study are available from the corresponding author upon reasonable request.

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