ejpmr, 2025, 12(2), 561-566

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

REVIEW OF DIOSGENIN AND ITS PHARMACOLOGICAL EFFECTS

Aditi Rajaendra Waghmare*[1], Astikta Ashok Bhondave[2], Dr. Hemant V. Kamble[3] and S. R. Ghodake[4]

[1,2]Student, Department of Pharmacology, LSDP College of Pharmacy, Pune, Maharashtra.
[3]Principal, Department of Pharmacology, LSDP College of Pharmacy, Pune, Maharashtra.
[4]Professor, Department of Pharmacology, LSDP College of Pharmacy, Pune, Maharashtra.

***Corresponding Author: Aditi Rajaendra Waghmare**

Student, Department of Pharmacology, LSDP College of Pharmacy, Pune, Maharashtra.

Article Received on 27/12/2024 **Article Revised on 17/01/2025** **Article Accepted on 06/02/2025**

ABSTRACT

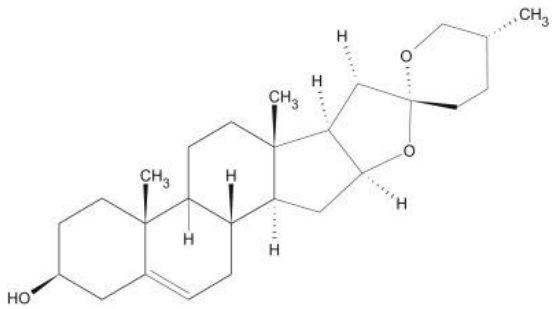
Diosgenin is a steroidal sapogenin, which has been proven to have various pharmacological effects such as anti-cancer, anti diabetic, anti-inflammatory,immune system modulating effects, anti-thrombotic, antiasthmatic, hepatoprotective, anti-atherosclerosis, hypolipidemia and antioxidative and neuroprotective effects. This review is to summarize the sources, Bioavailability and Pharmacokinetic Studies,it shows promising pharmacological effects of diosgenin, clinical studies investigations have demonstrated diosgenin's nontoxic nature and Toxicological Profile in which the discuss the Safety profile of diosgenin. Aiming to provide detailed information for the further development and application of diosgenin, which is important to improve the utilization value of diosgenin.

KEYWORDS: Diosgenin(DG), steroidal sapogenin, Pharmacological effects, safety profile.

INTRODUCTION

The effectiveness of natural medicines derived from medicinal herbs, plants, vegetables, and fruits in treating and preventing various human ailments. These include obesity, neurological disorders, cancer, metabolic syndromes, cardiovascular disease, and diabetes. the various natural products as a source of safe drugs for the treatment of various ailments in humans.[1]

Diosgenin (3β-Hydroxy-5-spirostene) is a herbal phytosteroid sapogenin found in several plant families, such as Liliaceae, Dioscoreaceae, Scrophulariaceae, Solanaceae, Leguminosae, Agavaceae, Rhamnaceae, and Amaryllidaceae. Diosgenin possesses numerous biochemical and physiological functions. Diosgenin has received a considerable amount of attention in recent years owing to its effectiveness in the treatment of numerous diseases, namely, cardiovascular diseases,cancer, neurological disorders, diabetes, and hyperlipidemia, in addition to its anti-inflammatory and antioxidant properties.[2]



Structure of Diosgenin

Molecular Formula of Diosgenin: C27H42O3

Sources of Diosgenin

Diosgenin (DG) is primarily derived from Dioscorea species, Heterosmilax species, and Trigonella foenum-graecum (fenugreek), with high levels found in wild yams like Dioscorea villosa. A total of 137 Dioscorea species contain Diosgenin, 41 of which have more than 1%. Other significant sources include Dioscorea zingiberensis, Trillium govanianum, and Costus speciosus, which contain up to 2.5% Diosgenin. Diosgenin is typically produced by hydrolyzing steroidal saponins using strong acids, bases, or enzymes. Microbial transformation is emerging as an eco-friendly, cost-effective method for Diosgenin production due to its mild reaction conditions and specificity.[3]

Bioavailability and Pharmacokinetic Studies of Diosgenin

Pharmacokinetic studies on diosgenin (DG) showed that after oral administration in rats, DG reached peak plasma concentrations at 5 hours with a bioavailability of 4.45%. It was mainly excreted in feces and rapidly eliminated via bile. DG distributed primarily to the liver, adrenals, and gastrointestinal walls. In humans, a 3 g/day dose of DG for four weeks did not significantly change serum levels. Metabolites, including monohydroxylated diosgenin, were found in the bile of rats and dogs.[4],[5]

Pharmacological effects of diosgenin

Anti-tumor effects

Diosgenin shows strong anti-cancer properties by inhibiting cancer cell growth, inducing apoptosis, and suppressing metastasis in vitro and in vivo. It works by increasing reactive oxygen species, inducing autophagy, and disrupting key signaling pathways like mTOR. Despite promising results in animal models, its poor solubility and low bioavailability limit its therapeutic potential, requiring further research for clinical use.[6],[7]

Diosgenin inhibits tumor growth, causes DNA fragmentation, and induces apoptosis in animal cancer models. In a mouse xenograft model, it effectively reduced tumor growth, both alone and in combination with thymoquinone (TQ).[8]

Effects on breast cancer

Breast cancer, a common and increasingly prevalent malignancy in women, is influenced by age and poor lifestyle factors. Studies show that diosgenin significantly inhibits breast cancer, particularly by inducing apoptosis. In experiments with the human breast cancer cell line MCF-7, diosgenin effectively reduced cell proliferation, invasion, and migration.[9]

Effects on liver cancer

Hepatocellular carcinoma (HCC) is a highly malignant cancer with a rising incidence and poor early diagnosis, often diagnosed in later stages with metastatic tumors. Diosgenin has shown potential in preventing and delaying liver cancer by inhibiting cell growth. It induces apoptosis through cell cycle arrest, particularly at the G2/M phase, in HCC cells (Bel-7402, SMMC-7721, HepG2). Diosgenin's effects include upregulation of p21 and p27 proteins and activation of cystathionin, contributing to its anti-cancer action.[10]

Effects on gastric cancer

Diosgenin inhibits the proliferation of gastric cancer cells by reducing the proliferative activity of human umbilical vein endothelial cells (HUVEC), thereby inhibiting intratumor angiogenesis and disrupting the blood supply to the tumor.[11]

Glioblastoma

Dioscin has shown significant antitumor activity both in vitro and in vivo. It inhibits the growth of C6 glioma cancer cells, reduces tumor size, and extends the lifespan of rats. The mechanism of action involves promoting the accumulation of reactive oxygen species (ROS), inducing DNA damage, and triggering mitochondrial-mediated apoptosis signaling.[12]

Anti-diabetic effects

Diosgenin is a compound with significant anti-diabetic properties, promoting better blood sugar control and improving insulin sensitivity. It enhances insulin secretion from pancreatic beta cells, boosts glucose uptake in muscle and fat tissues, and inhibits the enzyme alpha-glucosidase, which slows carbohydrate digestion. Diosgenin also combats oxidative stress, supports lipid metabolism by reducing cholesterol, and may reduce inflammation related to diabetes.[13],[14]

Immunomodulation and anti-inflammation

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by inflammation of the synovial joints, which can lead to the destruction of cartilage and bone. This often results in abnormal joint damage, particularly in severe cases. Recent research has explored the effects of diosgenin, a natural compound, on immune regulation and inflammation in hiRA. The studies indicate that diosgenin can modulate immune cells and transfer factors in collagen-induced arthritis (CIA) mice, demonstrating immunosuppressive properties that help reduce inflammatory responses, potentially offering therapeutic benefits for managing RA.[15]

Anti-thrombotic effects

Diosgenin has potential therapeutic effects in managing thrombophilia, a vascular disease that affects blood circulation. It inhibits platelet aggregation by increasing nitric oxide (NO) levels, reduces myocardial infarction size, and lowers blood viscosity, contributing to anti-thrombotic activity. Diosgenin also improves anticoagulation by prolonging clotting times (APTT, PT, and TT), helping prevent thrombosis, as demonstrated in a mouse thrombosis model.[16]

Antiasthmatic effects

A study by Junchao and colleagues explored the anti-asthmatic effects of diosgenin using ovalbumin-induced asthmatic mice and primary tracheal epithelial cells. The results showed that diosgenin significantly reduced the secretion of inflammatory factors such as TNF-α, IL-1β, and IL-6. This effect was mediated by the upregulation of glucocorticoid receptors and various anti-inflammatory proteins, alongside the downregulation of heat shock proteins (HSP70).[17]

Hepatoprotective effects

Fenugreek seeds are a primary source of diosgenin, which has been shown to exert hepatoprotective effects in diabetic rats. Both fenugreek seed extract and diosgenin help reduce liver enzyme levels, triglycerides, lipid peroxidation, and ER stress markers. They also increase liver antioxidant activity and glycogen content.

Histological analysis indicates that these treatments alleviate liver damage caused by type 2 diabetes. The positive effects are believed to result from the normalization of oxidative stress and ER stress.[2]

Diosgenin, a compound studied for its hepatoprotective effects, has shown potential in treating liver fibrosis. Xie et al. found that diosgenin significantly inhibited the proliferation of hepatic stellate cells induced by TGF-β1. It also reduced the expression of collagen I, alpha-smooth muscle actin, and TGF-β receptors I and II. Furthermore, diosgenin downregulated TGF-β1-induced phosphorylation of Smad3 in these cells, suggesting its potential as an antifibrotic agent for liver diseases, including those caused by alcohol consumption, viruses, or obesity-related conditions.[18]

Anti Atherosclerosis effects

The potential of diosgenin and its derivatives in preventing atherosclerosis was explored by several researchers. Specifically, Lv and their team investigated the therapeutic effects of diosgenin on macrophage cholesterol metabolism and its underlying mechanisms.[19]

Hypolipidemia and Antioxidative effects

the hypolipidemic (cholesterol-lowering) and antioxidative effects of diosgenin in rats fed a high-cholesterol and high-fat diet. The researchers also explore the molecular mechanisms behind diosgenin's protective effects on blood vessels, focusing on oxidative stress-induced vascular apoptosis (cell death). They found that diosgenin can reduce oxidative stress and prevent apoptosis in human vascular endothelial cells (HUVECs) caused by hydrogen peroxide (H2O2). The protective effects are primarily attributed to diosgenin's regulation of mitochondrial dysfunction pathways, helping to counteract the damage that would otherwise lead to endothelial cell death.[20]

Neuroprotective effects

Alzheimer's Disease and Parkinson's Diseases.

Alzheimer's Disease (AD) is a neurodegenerative disorder involving cognitive decline, with key mechanisms such as amyloid-β (Aβ) accumulation and tau hyperphosphorylation. Diosgenin (DG) and its derivatives show promise in reducing Aβ plaques, improving memory, and decreasing tau hyperphosphorylation in animal models. Compound 6 (diosgenin 3-caproate) has been particularly effective in protecting neurons from Aβ toxicity and mitochondrial impairment. Additionally, diosgenin-curcumin conjugates demonstrate neuroprotective effects by inhibiting Aβ oligomer formation and exhibiting antioxidant activity.[21]

In Parkinson's Disease (PD), DG has shown protective effects against motor deficits induced by lipopolysaccharide (LPS) in rats, and diosgenin derivatives like Compound 11 have exhibited neuroprotective properties by reducing apoptosis and promoting angiogenesis. These findings suggest DG and its derivatives as promising candidates for treating neurodegenerative diseases like AD and PD.[22]

Cognitive Effects.

Diosgenin (DG) has been shown to help improve cognitive function in various situations involving memory loss or cognitive decline. Studies found that DG can boost antioxidant activity in aging mice, helping to reverse learning and memory problems. It has also been shown to protect brain cells from damage caused by oxidative stress, which is common in conditions like HIV-related dementia. DG seems to help reduce the harmful effects of certain proteins linked to brain damage. Additionally, a compound related to DG from a specific plant improved learning and memory in aging rats, possibly by helping to fix problems with cell recycling in the brain. These findings suggest DG could be helpful for improving cognitive health and addressing age-related cognitive issues.[23]

Neuroinflammation

Diosgenin (DG) and its derivatives have shown promise in addressing neuroinflammation, which plays a critical role in neurodegenerative diseases. Overactivation of microglia and the overproduction of inflammatory cytokines are common in such disorders. Several studies have highlighted DG's potential to reduce this inflammation and protect cognitive function.[24]

Multiple Sclerosis.

Diosgenin (DG) shows promise as a therapeutic agent for multiple sclerosis (MS), a chronic inflammatory disease of the central nervous system. Research in an experimental autoimmune encephalomyelitis (EAE) mouse model showed that DG reduced inflammation, demyelination, and microglial activation, while also suppressing T cell proliferation. DG promoted the differentiation of oligodendrocyte progenitor cells into mature oligodendrocytes, aiding remyelination in a cuprizone-induced demyelination model. These findings suggest DG could be an effective treatment for MS by reducing inflammation and enhancing remyelination.[25]

Spinal cord injury

Spinal cord injury (SCI) is a serious neurological condition that often results in permanent disability, motor deficits, and sensory loss. Few effective treatments are currently available for SCI. However, research by Chen et al. showed that a diosgenin (DG)-rich extract from *Trillium tschonoskii Max* has a neuroprotective effect in rats with SCI. This effect is attributed to the upregulation of ciliary neurotrophic factor (CNTF) and its receptor (CNTFRα) at both mRNA and protein levels, which may help support spinal cord recovery.[26]

Stroke and Thrombosis

Stroke is a major public health issue, with ischemic stroke being the most common type. Research by Zhu et

al. showed that Compound 3, derived from diosgenin, has therapeutic potential for ischemic stroke in rats. It reduces infarct volume and neurological deficits by inhibiting inflammatory responses through the TLR4/MyD88/NF-κB signaling pathway.[27]

Thrombosis, especially in cerebral arteries, is a leading cause of death and disability. Zhang et al. developed diosgenin-based saponins, including Compound 5, which demonstrated strong antithrombotic effects. Compound 5 helped prolong bleeding time and inhibit platelet aggregation in rats, although the exact mechanism requires further investigation.[28]

Cerebral Brain Ischemia-Reperfusion Injury

Cerebral ischemia-reperfusion (I/R) injury occurs when blood supply to the brain is restored after ischemia, leading to brain damage. Diosgenin (DG) has shown promise in treating this injury in rat models. DG administration before surgery improved motor function, reduced brain damage, decreased apoptosis, and suppressed inflammation by blocking the NF-κB pathway, suggesting its potential as a treatment for ischemic stroke.[29]

Antidepressant Effects

Diosgenin (DG) shows antidepressant potential. In studies, chronic DG administration improved depressive behavior in high-anxiety rats by modulating the neuroimmune system.[30]

Neuropathic Pain

Neuropathic pain, often caused by conditions like diabetes and brain l injury, is resistant to treatment. found that diosgenin (DG) reduced pain in rats with chronic constriction injury (CCI) by inhibiting key inflammatory pathways (p38MAPK and NF-κB), reducing proinflammatory cytokines and oxidative stress, ultimately alleviating pain symptoms.[31]

Clinical Studies

A clinical study of the effects of a DG-rich yam extract on cognitive enhancement in 28 healthy volunteers aged 20 to 81 years. After 12 weeks of administration, the extract significantly improved semantic fluency without any adverse effects, suggesting that DG can enhance cognitive function in healthy adults.[32]

Toxicological Profile: Safety and Side Effects

Diosgenin is generally considered safe at doses up to 562.5 mg/kg, with no harmful effects observed in certain studies. However, higher doses (1125 mg/kg or more) of steroidal saponins, which include diosgenin, can cause toxicity and even death. Diosgenin has shown selective toxicity to cancer cells without affecting normal cells, and it also demonstrates antithrombotic properties similar to aspirin, with reduced bleeding risks. Additionally, diosgenin has a mild inhibitory effect on cytochrome P450 enzymes, suggesting minimal drug interactions and low toxicity when used alongside other medications.[33]

CONCLUSION

The study highlights diosgenin as an important natural pharmaceutical compound with significant pharmacological effects such as antitumor, anti-diabetic, hypolipidemia, hepatoprotective, immunomodulatory, anti-inflammatory, neuroprotective and anti-thrombotic. Extensive research has demonstrated the potential of diosgenin and its derivatives, suggesting the need for further studies to explore its pharmacological properties and underlying mechanisms. Such research could pave the way for diosgenin's clinical application in treating human diseases. In conclusion, diosgenin holds considerable value and is expected to receive increasing attention from the scientific community for its therapeutic potential.Diosgenin's nontoxic nature supports its potential inclusion in upcoming clinical studies and trials. It shows promise for the treatment and prevention of various chronic diseases. The ongoing investigation into diosgenin's therapeutic potential is expected to provide stronger evidence for its clinical application.

REFERENCES

1. D. J. Newman and G. M. Cragg, “Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019,” Journal of Natural Products, 2020; 83(3): 770–803.
2. Parvaneh Mohseni-Moghaddam, Manijeh Khanmohammadi, and Mehrdad Roghani. "Hepatoprotective Effects of Diosgenin: Possible Mechanisms of Action." Frontiers in Pharmacology, 2023; 14: 1226548.
3. Cai, B., Zhang, Y., Wang, Z., Xu, D., Jia, Y., Guan, Y., Liao, A., Liu, G., Chun, C. J., & Li, J. (2020). Therapeutic potential of diosgenin and its major derivatives against neurological diseases: Recent advances. Oxidative Medicine and Cellular Longevity, 2020; 3153082.
4. M. Okawara, Y. Tokudome, H. Todo, K. Sugibayashi, and F. Hashimoto, “Effect of β-cyclodextrin derivatives on the diosgenin absorption in Caco-2 cell monolayer and rats,” Biological & Pharmaceutical Bulletin, 2014; 37(1): 54–59.
5. M. Okawara, Y. Tokudome, H. Todo, K. Sugibayashi, and F. Hashimoto, “Enhancement of diosgenin distribution in the skin by cyclodextrin complexation following oral administration,” Biological & Pharmaceutical Bulletin, 2013; 36(1): 36–40.
6. Wang, H., Hu, J. H., Liu, C. C., Liu, M., Liu, Z., & Sun, L. X. (2018a). Analysis of antitumor mechanism of diosgenin by cell metabonomics strategy. Chinese Journal of Experimental Traditional Medical Formulae, 24: 95-101.
7. Jiang, S., Fan, J., Wang, Q., Ju, D., Feng, M., Li, J., Guan, Z. B., An, D., Wang, X., & Ye, L. (2016).

Diosgenin induces ros-dependent autophagy and cytotoxicity via mtor signaling pathway in chronic myeloid leukemia cells. Phytomedicine, 23(3): 243-252. http://dx.doi.org/10.1016/j.phymed.2016.01.010. PMid:26969378.

8. Das, S., Dey, K. K., Dey, G., Pal, I., Majumder, A., MaitiChoudhury, S., Kundu, S. C., & Mandal, M. (2012). Antineoplastic and apoptotic potential of traditional medicines thymoquinone and diosgenin in squamous cell carcinoma. PLoS One, 7(10): e46641. http://dx.doi.org/10.1371/journal.pone.0046641. PMid:23077516.
9. Li, Y., Lyu, P., Hou, L., Zhang, Y., Wang, C., Fan, Q., Chen, X., & Shi, F. (2019). Diosgenin's inhibitory effects on proliferation and migration of MCF-7 breast cancer cells through demethylation of microRNA-145. Journal of Beijing University of Traditional Chinese Medicine, 42(8): 662-666.
10. Li, Y., Wang, X., Cheng, S., Du, J., Deng, Z., Zhang, Y., Liu, Q., Gao, J., Cheng, B., & Ling, C. (2015). Diosgenin induces G2/M cell cycle arrest and apoptosis in human hepatocellular carcinoma cells. Oncology Reports, 33(2): 693-698. http://dx.doi.org/10.3892/or.2014.3629. PMid:25434486.
11. Huo, Z. H., Hu, J., Chu, Z. L., Lv, S., Yin, P., & Zhang, L. (2014). Mechanism underlying inhibition of migration of gastric carcinoma by diosgenin in vitro and vivo. Journal of Jiangsu University, 24(5): 394-398.
12. L. Lv, L. Zheng, D. Dong et al., "Dioscin, a natural steroid saponin, induces apoptosis and DNA damage through reactive oxygen species: a potential new drug for treatment of glioblastoma multiforme," Food and Chemical Toxicology, 2013; 59: 657–669.
13. Sengupta, S., & Singh, R. (2017). Diosgenin: A promising anti-diabetic agent. *Journal of Diabetes & Metabolic Disorders, 16*(1): 1-10.
14. Sharma, R., & Bansal, A. (2015). Diosgenin and its therapeutic potential in diabetes. European Journal of Medicinal Chemistry, 89: 29-40.
15. Zhao, X. (2016). Effect of diosgenin on expression of Th1, Th2, Th17 cell and its specific transcription factors in collagen-induced arthritis mice in vitro. (Master Dissertation). Chengde Med Univ., Hebei.
16. Gong, G., Qin, Y., & Huang, W. (2011). Anti-thrombosis effect of diosgenin extract from dioscorea zingiberensis C.H. Wright in vitro and in vivo. Phytomedicine, 18(6): 458-463. http://dx.doi.org/10.1016/j.phymed.2010.08.015. PMid:21036572.
17. Y. Junchao, W. Zhen, W. Yuan et al., "Anti-trachea inflammatory effects of diosgenin from Dioscorea nipponica through interactions with glucocorticoid receptor α," Journal of International Medical Research, 2016; 45: 101–113.
18. W. L. Xie, R. Jiang, X. L. Shen, Z. Y. Chen, and X. M. Deng, "Diosgenin attenuates hepatic stellate cell activation through transforming growth factor-β/Smad signaling pathway," International Journal of Clinical and Experimental Medicine, 2015; 8(11): 20323–20329.
19. Y.-C. Lv, J. Yang, F. Yao et al., "Diosgenin inhibits atherosclerosis via suppressing the MiR-19b-induced downregulation of ATP-binding cassette transporter A1," Atherosclerosis, 2015; 240(1): 80–89.
20. Gong, G., Qin, Y., Huang, W., Zhou, S., Wu, X., Yang, X., Zhao, Y., & Li, D. (2010). Protective effects of diosgenin in the hyperlipidemic rat model and in human vascular endothelial cells against hydrogen peroxide-induced apoptosis. Chemico-Biological Interactions, 183(1): 119-125.
21. C. Tohda, T. Urano, M. Umezaki, I. Nemere, and T. Kuboyama, "Diosgenin is an exogenous activator of 1,25D3-MARRS/Pdia3/ERp57 and improves Alzheimer's disease pathologies in 5XFAD mice," Scientific Reports, 2012; 2(1).
22. D. Cai, J. Qi, Y. Yang et al., "Design, synthesis and biological evaluation of diosgenin-amino acid derivatives with dual functions of neuroprotection and angiogenesis," Molecules, 2019; 24(22): 4025.
23. C. S. Chiu, J. S. Deng, M. T. Hsieh et al., "Yam (Dioscorea pseudojaponica Yamamoto) ameliorates cognition deficit and attenuates oxidative damage in senescent mice induced by D-galactose," The American Journal of Chinese Medicine, 2009; 37(5): 889–902.
24. R. Yang, W. Chen, Y. Lu et al., "Dioscin relieves endotoxemia induced acute neuro-inflammation and protect neurogenesis via improving 5-HT metabolism," Scientific Reports, 2017; 7(1): 1–13.
25. W. Liu, M. Zhu, Z. Yu et al., "Therapeutic effects of diosgenin in experimental autoimmune encephalomyelitis," Journal of Neuroimmunology, 2017; 313: 152–160.
26. X. B. Chen, M. Y. Zhu, F. R. Qin et al., "Effect of extract of Trillium tschonoskii Maxim on ciliary neurotropic factor and its receptor α in rats suffering from spinal cord injury," Medical Journal of Chinese People's Liberation Army, 2015; 40: 622–626.
27. S. Zhu, S. Tang, and F. Su, "Dioscin inhibits ischemic stroke-induced inflammation through inhibition of the TLR4/MyD88/NF‑κB signaling pathway in a rat model," Molecular Medicine Reports, 2018; 17(1): 660–666.
28. R. Zhang, B. Huang, D. du et al., "Anti-thrombosis effect of diosgenyl saponins in vitro and in vivo," Steroids, 2013; 78(11): 1064–1070.
29. X. Zhang, X. Xue, J. Zhao et al., "Diosgenin attenuates the brain injury induced by transient focal cerebral ischemia-reperfusion in rats," Steroids, 2016; 113: 103–112.
30. Y. J. Ho, S. Y. Tai, C. R. Pawlak, A. L. Wang, C. W. Cheng, and M. H. Hsieh, "Behavioral and IL-2

responses to diosgenin in ovariectomized rats," The Chinese Journal of Physiology, 2012; 55(2): 91–100.
31. W. X. Zhao, P. F. Wang, H. G. Song, and N. Sun, "Diosgenin attenuates neuropathic pain in a rat model of chronic constriction injury," Molecular Medicine Reports, 2017; 16(2): 1559–1564.
32. C. Tohda, X. Yang, M. Matsui et al., "Diosgenin-rich yam extract enhances cognitive function: a placebo-controlled, randomized, double-blind, crossover study of healthy adults," Nutrients, 2017; 9(10): 1160.
33. Semwal, P., Painuli, S., Abu-Izneid, T., Rauf, A., Sharma, A., Daştan, S. D., Kumar, M., Alshehri, M. M., Taheri, Y., Das, R., Mitra, S., Emran, T. B., Sharifi-Rad, J., Calina, D., & Cho, W. C. (2021). Diosgenin: An updated pharmacological review and therapeutic perspectives. Phytotherapy Research, 35(5): 2551–2574.