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Letter to the editor:

AN UPDATE ON THE BIOLOGICAL AND PHARMACOLOGICAL ACTIVITIES OF DIOSGENIN

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Dear Editor,

Diosgenin, a phytosteroid saponin, is found at high levels in several plant species, including *Costus speciosus*, *Smilax menispermoidea*, *Trigonella foenum*, species of *Paris*, *Aletris*, *Trigonella*, and *Trillium*, and many species of *Dioscorea* (Patel et al., 2013; Chen et al., 2011).

Fujii and Matsukawa first discovered diosgenin within *Dioscorea tokoro* Makino in 1935 (Djerassi et al., 1952). The biosynthesis of steroidal saponins such as diosgenin in plants has not yet been reported in detail, although cholesterol was found to be a precursor of this compound. Cholesterol is formed from lanosterol and some of the reactions involved are catalyzed by cytochrome P450 systems. Vaidya et al. (2013) suggested that diosgenin might be formed from squalene-2,3-oxide in two ways: from lanosterol via cholesterol, and from cycloartenol via the formation of sitosterol (Ciura et al., 2017).

In the pharmaceutical industry, diosgenin is the principal precursor compound in the manufacture of several synthetic steroidal drugs (Chen et al., 2015). It also represents a promising bioactive biomolecule that exhibits various biological properties; these include hypolipidemic, hypoglycemic, antioxidant, anti-inflammatory, and antiproliferative activities (Jesus et al., 2016). Diosgenin has therefore attracted considerable attention in recent years within the pharmaceutical, functional food, and cosmetic industries. Here, we summarize recent studies performed to evaluate the biological and pharmacological activities of diosgenin (Table 1).

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Table 1: Recent studies of the biological and pharmacological activities of diosgenin

Key findings	Reference
Diosgenin selectively suppressed the production/expression of pro-inflammatory M1 markers by activated microglia, without affecting M2 markers, and might provide neuroprotection by regulating microglial M1 polarization.	Wang et al., 2017
Diosgenin inhibited resilient breast cancer stem cells. This could provide a rationale for the development of diosgenin-based therapies for breast cancer.	Bhuvanalakshmi et al., 2017
Diosgenin inhibited angiotensin II-induced extracellular matrix remodeling in rat cardiac fibroblasts by suppressing the transforming growth factor-β1/Smad3 signaling pathway. Diosgenin may therefore possess therapeutic potential for the treatment of cardiac fibrosis.	Zhou et al., 2017
Diosgenin improved skin collagen levels by shifting the fibroblast dynamics from proliferation to differentiation via cell cycle arrest.	Haratake A et al., 2017
Diosgenin played a protective role against osteoarthritis by activating the sirtuin type 1 signaling pathway, inhibiting chondrocyte apoptosis, and increasing chondrocyte mitochondrial oxidative stress capacity.	Liu et al., 2017
High glucose-induced myocardial injury was prevented using morroniside and/or diosgenin, which reduced oxidative stress and apoptosis in rat cardiomyocytes. Morroniside plus diosgenin produced a stronger effect than either compound alone.	Pi et al., 2017
Diosgenin suppressed the secretion of tumor necrosis factor-α, interleukin-1β, and interleukin-6, enhanced the expression of glucocorticoid receptors, SLPI (secretory leukocyte protease inhibitor), GILZ (glucocorticoid-induced leucine zipper), and MKP-1 (mitogen-activated protein kinase phosphatase-1), and inhibited the expression of HSP70. These findings could provide some valuable information on the molecular mechanism underlying the effects of diosgenin, which might facilitate its clinical application.	Junchao et al., 2017
Administration of diosgenin to allergic mice greatly enhanced the induction of T helper 1-like regulatory T cells, suggesting a role for these cells in the anti-allergic effects of diosgenin against T helper 2-type allergies.	Huang et al., 2017
Structure-activity analyses indicated that diosgenin analogues with a simple phenyl R moiety or electron-withdrawing ortho-substituted R moieties showed improved anti-proliferative activities.	Masood-Ur-Rahman et al., 2017
The combination of diosgenin with an autophagy inhibitor may be an effective strategy to increase the antitumor effect of diosgenin.	Nie et al., 2016
Sterol regulatory element-binding transcription factor-1 appeared to be a major target of diosgenin and mediated its anti-diabetic activities in gestational diabetes. This information provided an insight into the biological activities of diosgenin and will provide novel opportunities to investigate its anti-diabetic activities.	Hua et al., 2016
Diosgenin inhibited apoptosis and increased the mitochondrial oxidative stress capacity of chondrocytes in mice with osteoarthritis; this effect was closely related to Janus kinase 2/signal transducer and activator of transcription 3 signaling pathway activation.	Liu et al., 2016
Diosgenin inhibited testosterone propionate-induced prostate enlargement and may be a candidate agent for the treatment of benign prostatic hyperplasia.	Chen et al., 2016
Diosgenin and 5-methoxypsoralen improved insulin resistance via an estrogen receptor-mediated phosphatidylinositol 3-kinase/Akt activation pathway. This might provide a new approach to the treatment of type 2 diabetes mellitus, especially for women with low estrogen levels.	Fang et al., 2015
Diosgenin enhanced eryptosis, shrinking erythrocytes and scrambling phospholipids in the erythrocyte cell membrane. This was associated with Ca^{2+} entry, oxidative stress, and ceramide.	Mischitelli et al., 2016

Key findings	Reference
Diosgenin was neuroprotective against ischemia-reperfusion-induced injury. This effect involved anti-apoptotic and anti-inflammatory activity, and modulation of nuclear factor-κB signaling pathway properties.	Zhang et al., 2016
Compound 5, a new derivative of diosgenin, exhibited antithrombotic activity, mainly by reducing platelet aggregation and regulating factor VIII. This effect was comparable to that of aspirin, but with fewer side effects.	Zheng et al., 2016
Diosgenin increased compact bone formation and probably inhibited cancellous bone resorption, which led to an improvement of the mechanical properties of compact and cancellous bone.	Folwarczna et al., 2016
Diosgenin treatment successfully suppressed phthalic anhydride-induced skin inflammation in interleukin-4/ luciferase/CNS-1 (the enhancer of interleukin-4) transgenic mice by reducing expression of interleukins -4 and -6, and reducing the immunoglobulin E level and mast cell infiltration.	Kim et al., 2016
Diosgenin increased the generation of reactive oxygen species and this was cytotoxic to chronic myeloid leukemia cells, while also inducing autophagy. Autophagy functions as a cytoprotective mechanism to reduce the cytotoxicity of diosgenin in tumor cells; inhibition of autophagy can thus enhance the anti-chronic myeloid leukemia activity of diosgenin.	Jiang et al., 2016
Diosgenin prevented bone loss in experimental rats by increasing the level of estradiol, reducing bone turnover.	Zhao et al., 2016
Diosgenin inhibited proliferation and activation of hepatic stellate cells-T6 cells, at least in part, via the transforming growth factor-β1/Smad signaling pathway. These results indicated that diosgenin may have the potential to treat liver fibrosis.	Xie et al., 2015
Diosgenin reduced age-associated changes in femur microarchitecture and morphology in senescence-accelerated OXYS rats, suggesting that diosgenin may have beneficial effects on aging-induced osteoporosis.	Tikhonova et al., 2015
Diosgenin isolated from *Costus speciosus* showed anticancer and pro-apoptotic effects on cancer cell proliferation.	Selim and Al Jaouni, 2015
Diosgenin inhibited interleukin-1β-induced expression of inflammatory mediators, indicating that it could be used as a potential treatment for osteoarthritis.	Wang et al., 2015
Diosgenin modulated the opening of mitochondrial ATP-sensitive potassium channels and reduced oxidative stress. These activities could contribute to the cardioprotective effect of diosgenin in ischemia-reperfusion-induced injury.	Badalzadeh et al., 2015
Diosgenin enhanced ATP-binding cassette transporter of A1-dependent cholesterol efflux and prevented aortic atherosclerosis progression by reducing the expression of macrophage miR-19b.	Lv et al., 2015
Hypercholesterolemia and hepatosteatosis were prevented by diosgenin-mediated modulation of enzymes associated with cholesterol metabolism.	Hao et al., 2015
Diosgenin showed the potential to produce anti-diabetic effects that mitigated hyperglycemia and insulin resistance, as well as alleviating metabolic dysregulation of the lipid profile in both plasma and tissues.	Naidu et al., 2015

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Conflict of interest

The authors declare no conflict of interest.

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