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Action of diosgenin and homoeopathic pathogenesis of *Dioscorea villosa*

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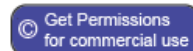
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Abstract

Background: *Dioscorea villosa* is a popular herbal remedy for pains. Early Americans used this to treat colic which is also established in homoeopathic proving and verified clinically along with other important phenomena. Diosgenin is its primary active ingredient. It has been investigated that all possible revealed actions of this plant are due to this ingredient. **Objective:** The aim of this study is to understand pathological background and prescribing areas of *D. villosa* by correlating and analyzing Homoeopathic pathogenesis with the knowledge of pathophysiological activities of Diosgenin. **Study Method:** Information was collected from various researches on animal and human models regarding actions of Diosgenin. Homoeopathic pathogenesis of *D. villosa* have been studied and analyzed from 'The Guiding Symptoms of our Materia Medica' by C. Hering and also from the experiences of different authors to find pathological background as well as prescribing areas of *D. villosa* by correlating with the actions of Diosgenin.

Result: Diosgenin has prominent action on cholesterol metabolism, hormones (oestrogen and dehydroepiandrosterone [DHEA]), inflammations, and allergic activities on animal and human models. These pathological actions of Diosgenin have similarity with the pathological background of homoeopathic pathogenesis of *D. villosa*. **Conclusion:** Actions of Diosgenin reflect in the homoeopathic pathogenesis of *D. villosa* such as altered cholesterol metabolism, irregularity of hormonal (DHEA and estrogen) functions, and anti-inflammatory and anti-allergic phenomena with their related manifestations. Moreover, these might be the underlying pathological essence of this drug.

Keywords: Anti-allergic, Anti-cancerous, Anti-diabetic, Anti-inflammatory, Cholesterol metabolism, Dehydroepiandrosterone-oestrogen, *Dioscorea villosa*, Diosgenin, Homoeopathic pathogenesis

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In this article

Abstract

Introduction

Action of Diosgenin

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Introduction

Dioscorea villosa (Wild Yam) is named after the Greek Physician Dioscorides of the 1st century. It contains saponins, namely Dioscin, which gives Diosgenin on hydrolysis. It is the precursor for synthesis of steroidal hormones. It also contains Dioscorin as an alkaloid.

Diosgenin is considered as the primary active ingredient. Dioscin has similar or overlapping effects to Diosgenin, but there has been little investigation done on the effects of Dioscin alone, Dioscorin has no known physiologic effects. Diosgenin is structurally similar to cholesterol.^[1]

Due to structural similarity, its action on cholesterol metabolism is not only hypothesized but has also been proven in several research studies. Diosgenin promotes fecal cholesterol excretion by inhibiting intestinal cholesterol absorption and enhancing biliary secretion.^[2]

Diosgenin has oestrogen properties. It may bind with oestrogen receptors of hypothalamus and takes part in negative feedback mechanism of estrogen control.^[3]

Wild yam is considered as a precursor to dehydroepiandrosterone (DHEA). DHEA supplements are manufactured from it and considered as a valid source, but the exact mechanisms of its conversion toward hormones *in vivo* are unknown. Some research studies proved its activity suggesting the same.^{[4],[5],[6]}

In several studies conducted in animal and human models, it has significant anti-inflammatory, anti-allergic, anti-diabetic, anti-cancerous properties as well.

Action of Diosgenin

Action in cholesterol metabolism

From several studies, it has been found that Diosgenin has the following properties related to cholesterol metabolism.

In animal models, it has been found that it inhibits cholesterol absorption.^{[7],[8]} Side by side, it increases biliary cholesterol secretion and output as well as altered serum cholesterol levels,^{[8],[9],[10]} increases fecal excretion of cholesterol, decreases plasma cholesterol levels,^{[11],[12]} decreases low-density lipoprotein (LDL) cholesterol, and elevates high-density lipoprotein (HDL) cholesterol.^[13] Not only that, it may also protect from bile salt toxicity.^[14] In human model, it has been found that Diosgenin can decrease triglycerides and phospholipids but increase serum HDL.^[15] In another study in mice model, Diosgenin significantly decreased serum total cholesterol level while slightly increased HDL level and also found protective effect against atherosclerosis by regulating pro-inflammatory mediators in serum.^[16]

Action on oestrogen and dehydroepiandrosterone

Although there is no such direct evidence of conversion of Diosgenin into any hormone, several studies suggest its oestrogen property.^[17] This property can be established by its binding with estrogen receptors of the hypothalamus as a part of negative feedback mechanism of estrogen control.

It significantly increased DHEA level in another study on rats!^[18]

Action on inflammations and allergic activities

It has significant anti-inflammatory activity as found in different studies in animal models as on sub-inflammatory intestinal inflammation in indomethacin-induced intestinal inflammation in rats,^[19] showing immunosuppressive effects by reducing the production of inflammatory mediators.^[20] It also has regulatory action on T-cell immunity in intestine of mice with food allergy,^[21] suppressive action of immunoglobulin E production on allergen-induced intestine inflammation, and mast cell infiltration and degranulation of food allergy in a murine model.^[22] It is also found that Diosgenin has significant anti-inflammatory activity by the inhibition of lipopolysaccharide-induced pro-inflammatory cytokines in a dose-dependent manner without any cytotoxicity^[23] and proved useful to ameliorate the inflammatory changes in obese adipose tissues.^[24]

Action in diabetes

It has anti-diabetic property involving glucose metabolism and might be a novel therapeutic agent.^{[25],[26]} In a study, it has been found that Diosgenin-induced increased DHEA may contribute to the improvement of hyperglycemia through muscular glucose transporter Type 4 signaling pathway activation in type 1 diabetes of rats.^[18]

Action in cancer

Different studies also revealed the action of Diosgenin on cancer. Several evidences suggest that it can reduce tumor multiplicity of adenoma or adenocarcinoma in colon,^{[27],[28]} breast adenocarcinoma,^{[29],[30]} hepatocellular carcinoma,^{[31],[32]} gastric cancer,^[33] prostate cancer,^[34] osteosarcoma^[35] etc

Homoeopathic Pat...

Associating Homo...

Prescribing Area...

Conclusion

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Important pathological conditions as well as manifestations of *D. villosa* from detailed recorded pathogenesis are seen in 'The Guiding Symptoms of our Materia Medica' by C. Hering^[36] and from the clinical description based on the experiences of pioneers like Dr. T.F. Allen,^[37] Dr. William H. Burt,^[38] Dr. J.C. Burnett,^[39] Dr. Samuel Lilienthal,^[40] Dr. P.N. Verma and Dr. Indu Vaid^[41] and others.

According to the proving of Dr. Gushing, there was dual action of *Dioscorea*. In primary effects as erotism and in secondary effects as impotency and both are attended by its peculiar type of spermatorrhea. Dr. Boyd reported that *Dioscorea* has curative property in spasmodic stricture of urethra with "pain about the umbilicus relieved by pressure; pressure on the rectum; and paroxysmal colic pains."^[42]

Gastrointestinal system

- Colic - Flatulent colic, bilious colic, and neuralgia of bowels with spasmodic pain in abdomen. Colic with feeble digestive power relieved by stretching the body out or by walking about. This modality has been considered as a characteristic feature of *Dioscorea*
- Diarrhoea and dysentery with colic
- Liver affection – Hard, dry, black stool indicates a diminution of bile, but large doses produce increased secretion of bile as indicated by the papery, yellow, loose stool^[38]
- Gall stone and much flatulence,^[40] along with feeble digestion.^[41]

Reproductive system

- Increased sexual excitement - constant sexual excitement, nocturnal emissions with amorous dreams, and erections when asleep, sometimes without erections. There is also diminished sexual desire with no erections for many days.
- Severe pain with cramp in flexor tendons of fingers and toes, alternating with false labor pains.

Vascular affections

- Haemorrhoids with constipation,^[38] Haemorrhoids with darting pain shooting to liver. It looks like bunches of grapes with great pain and distress^[37]
- Acute painful varicocele from excess venery or long-lasting unsatisfied desire^[39]

Heart affections

Angina pectoris, pains radiate into both arms.

Extremities

- Felons - early, when pains are sharp
- Sciatica right sided, shooting down thigh, <motion.



Effects of altered cholesterol metabolism

- Colic - Symptoms of biliary colic with flatulence and its character has underlying relation with the property of altered cholesterol metabolism
- Modality of colic - Pain while reclining and relieved by sitting up which is often retroperitoneal^[43]
- Pancreatic cause of abdominal colic - Pancreatic cause of abdominal colic and its affections can also be related to secondary cause of altered cholesterol metabolism or estrogenic effects^{[44],[45],[46]}
- Atherosclerotic affection of heart - Heart symptoms because of atherosclerotic changes in the arteries, which is due to the same altered cholesterol metabolism. It is found that Diosgenin has protective effect against atherosclerosis^[16]
- Atherosclerosis and sciatica - Atherosclerosis of arteries supplying the lumbar region has been suggested as a mechanism leading to inter-vertebral disc degeneration causing sciatica^[47]
- Hyperlipidemia and neuralgias. In a study, it has been identified that hyperlipidemia is a novel risk factor for peripheral neuropathies. It includes axonal distal polyneuropathy, vision and hearing loss, motor nerve system lesions, and sympathetic nervous system dysfunction.^[48]

Irregularities of hormonal functions

- Sexual excitement, vivid dreams, and emissions - In sexual sphere, action of DHEA can be related to vivid dreams and emissions. However, in a recent study, it has been found that reducing estrogen in men undergoing treatment for low testosterone resulted in a drop in libido and an increase in body fat, even as testosterone levels improved [49]
- False labor-like pain - Oestrogen has a property to induce the formation of oxytocin receptors in the uterus and make uterus sensitive to oxytocin for expulsion of fetus. Moreover, it also established that oxytocin receptor expression is being modulated by stimulation with estrogen not only in the pregnant but also in the nonpregnant uterus. Hence, estrogenic activity of *Dioscorea* not only facilitates labor by increasing oxytocin receptors density in uterus but it is also responsible for uterine contractility-associated disorders of the nonpregnant uterus [50]
- Constipation - Oestrogen has a significant role to develop constipation [51]
- Chronic venous diseases - In a recent study, it was also found that estrogen receptors play an important role in chronic venous diseases [52]
- Urethral stricture - In case of male, a large amount of estrogen cause atrophy and fibrosis of the spongy and cavernous bodies of the penis, depriving the urethra of its normal elasticity, which results in stricture. [53]

Anti-allergic and anti-inflammatory actions

- Diarrhoea or dysentery with colic - Abdominal colic with bowel complaints related to Diarrhoea or dysentery might be related to food allergy [22]
- Panaritium or felon - Symptoms of peripheral inflammatory changes in the form of panaritium might be related to the anti-inflammatory property of Diosgenin. It can also be explained from the pathology of hypercholesterolemia. It has been found that hypercholesterolemia is also associated with lymphatic vascular changes, leads to obstruction of lymphatic drainage. As a result of that, lack of protective body immune response may maintain this infection as well as inflammatory process. [54]

Prescribing Areas Revealed from Analyzed Homoeopathic Pathogenesis and Also from Different Actions of Diosgenin

1. Biliary, flatulent, or neurogenic colic of abdomen
2. Gall stone
3. Intestinal allergic or inflammatory affections with diarrhea, dysentery, and colic
4. Hypercholesterolemia or dyslipidemia and related manifestations, including atherosclerotic affections of heart and vascular system, peripheral vascular affection such as claudication
5. Complaints or manifestations related to DHEA and estrogen hormonal irregularities including sexual erotism or impotency with spermatorrhea
6. Oestrogen effects on venous system such as constipation with hemorrhoids, varicocele
7. Urethral stricture
8. Neuralgia
9. Diabetes
10. Cancer - Colon tumors (adenoma-adenocarcinoma); breast adenocarcinoma (HER2 oncoprotein-overexpressing AU565 human {also in MCF-7 and MDA-231}); hepatocellular cancer; gastric cancer; prostate cancer; and in osteosarcoma. [27],[28],[29],[30],[31],[32],[33],[34],[35]

Co-existence of manifestations derived from or associated with pathological essence of *Dioscorea* such as altered cholesterol metabolism, irregular hormonal (estrogen-DHEA) actions, allergic and inflammatory activities are the basis of homoeopathic approach as logical combination to prescribe *Dioscorea*. Similarly, characteristic pains or sensations, its extension, modalities, or other characteristic phenomena such as sexual dreams and spermatorrhea as stated by pioneers may represent individualizing features along with these underlying pathologies.

Conclusion

As expression and intensity of disease manifestations differ from one to another, drug pathogenesis revealed from homoeopathic proving and clinical experiments also differ because of individual's constitutional tendencies and susceptibility. However, inspite of these differing manifestations, the target areas and tendencies of the drug are definite. Similarly, drug actions on general or local physiological activities with altered function of internal factor(s) including hormone, enzyme, salt, or other bio-chemicals are also definite. In other words, varying degrees of intensity and differing modalities, sensations, extensions, or other modifications of resulting manifestations are developed from the definite altered physiological activities with affections of different bio-chemicals. These pathophysiological changes with altered function of bio-chemical or other factors are the pathological essence of medicine.

From the present study of *Dioscorea*, it can be identified that effect of pathological activity of Diosgenin shown in animal as well as in human models has similarity in the internal pathophysiological changes in homoeopathic pathogenesis of *D. villosa*. External signs and symptoms of these internal changes were expressed fragmentarily with individualistic differences throughout the recorded pathogenesis of this homoeopathic medicine.

Hence, it can be concluded that the underlying altered cholesterol metabolism, irregularity of hormonal (DHEA and estrogen) function, and anti-inflammatory and anti-allergic phenomena with their related manifestations are reflected as the pathological essence of *Dioscorea*. And

in the similar way of producing these pathological changes, Dioscorea has a capability to influence individual's homeostatic mechanism to maintain the normal state of these altered pathology and related phenomena.

In addition to the pathological complaints related to hypercholesterolemia or dyslipidemia, irregularity of estrogen and DHEA, future evaluation in the sphere of malignancies in colon, breast, hepatic, gastric, prostate, bones as well as for diabetes and intestinal allergic affections are to be considered for more clinical applicability of *Dioscorea* in homeopathic practice.

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Conflict of interest

None declared.

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Efficacy of Dioscorea villosa 6CH in treatment of dyslipidemia: A double-blind, randomized, placebo-controlled, clinical trial

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Dioscorea is a genus of flowering plants, and some Dioscorea species are known and used as a source for the steroidal sapogenin diosgenin. To screen potential resource from Dioscorea species and related medicinal plants for diosgenin extraction, a rapid method to compare the contents of diosgenin in various plants is crucial. An ultra-performance liquid chromatography (UPLC) coupled with diode array detection (DAD) and electrospray ionization mass spectrometry (ESI-MS) method was developed for identification and determination of diosgenin in various plants. A comprehensive validation of the de... Li X, Ma JZ, Shi YD: Research progress and prospects of Dioscorea and diosgenin. Chem Ind Forest Prod. 2010, 30: 107-112. Dioscorea villosa (wild yam) is native to North America and has been widely used as a natural alternative for estrogen replacement therapy to improve women's health as well as to treat inflammation, muscle spasm, and asthma. Diosgenin and dioscin (glycoside form of diosgenin) are reported to be the pharmacologically active compounds. Despite the reports of significant pharmacological properties of dioscin and diosgenin in conditions related to inflammation, cancer, diabetes, and gastrointestinal ailments, no reports are available on ADME properties of these compounds. This study was carri