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# MOJAVE YUCCA (*YUCCA SCHIDIGERA* ROEZL) EFFECTS ON FEMALE REPRODUCTION A REVIEW

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## ABSTRACT

**Yucca is an important source of biologically active substances such as steroidal saponins and stilbenes providing many beneficial effects when administered to humans and other animals. These substances offer a great potential in the prevention and treatment of current civilized diseases as well as to their: antioxidant, hypocholesterolaemic, anti-inflammatory, phytoestrogenic, pro-apoptotic, anti-proliferative, and anti-carcinogenic properties. This review focuses on the roles of two main yucca constituent groups and their ability to modulate ovarian functions and female reproductive performance. Both the biological activity of yucca substances and the mechanisms of their actions on ovaries are still incompletely understood. Thus, the direct effects of yucca extract on ovarian cells in animal models under *in vitro* conditions, as well as actions after yucca consumption will be discussed.**

**Key words: female reproduction; ovary; yucca (*Yucca schidigera* Roezl)**

## INTRODUCTION

In the past, yucca had great ethno-botanical importance for Native Americans in the southwestern regions of the USA and Mexico due to its remedial effects. Mojave yucca (*Yucca schidigera* Roezl; *Agavaceae*) extracts were used in folk medicine to relieve bleeding, joint pain, inflammatory processes in the male urogenital tract as well as skin problems [52]. Nowadays, yucca extract is widely used in cosmetics, pharmaceuticals, and in the food industries [57, 77]. It is widely used for improving the microclimate in breeding houses of several animal species [8]. The anti-deteriorating effect of yucca extract on food products is used for extending their shelf life [40, 57, 72]. Currently, yucca enjoys its comeback as a potential functional food in human nutrition and is commercially offered in various forms, such as capsules, herbal tea and beverages [52]. The consumption of yucca in any form can improve the functioning of many organs and tissues in the body through the activation or inhibition of various pathways.

Yucca is a source of many types of biologically active substances such as steroidal saponins and stilbenes [9, 78].

These constituents of yucca can act through: changing tissue metabolism, uptake of some chemical substances in the body, activation or competition of receptor ligands on cell membranes, prevention of oxidation of membrane lipids, as well as the activation of cell apoptosis and prevention of cell proliferation. Therefore, yucca have demonstrated many beneficial effects on animal and human organisms encompassing: anti-mutagenic [79], anti-inflammatory [4, 9, 37], anti-arthritic [9], hypocholesterolaemic in humans [27, 29], hens [3], goats [28], sheep [1, 80], and quails [2], hypoglycaemic [14], anti-proliferative and pro-apoptotic [4, 73], anti-platelet [46, 48], anti-microbial [43] and anti-carcinogenic [47] effects. Besides those beneficial effects on health, some adverse effects on the liver of rabbits after long-term (almost one year) consumption of yucca powder have occurred [15]. Moreover, the consumption of *Y. schidigera* extract may influence female reproduction by the modulation of ovarian functions; however, research studies for various animal models seem to be inconsistent and the data are not complete or sufficient to clarify the mechanisms of action.

Many articles have described the chemical structure of compounds contained in yucca powder [4, 9, 32, 37, 40, 48, 49, 56, 57, 65, 77]. For this reason, this current review will omit this topic and focus rather on the known and novel effects of *Y. schidigera* products and bioactive substances on female reproductive performance and ovarian functions. We will also briefly describe the main physiological actions of ovarian and their upregulating hormones. These known physiological pathways of hormone actions and the actions of yucca used in *in vivo* and *in vitro* studies (Table 1) provide us an outline of the possible mechanisms of how yucca could act on female reproduction.

**Saponins—representation and roles**

Yucca extracts are characterized by their strong foaming activity due to high (10—12 %) saponin content [21, 49]. Saponins of yucca bark are steroidal saponins, which include spirostanol and furostanol glycosides [32, 40, 49, 57, 77]. Spirostanol glycosides are predominant in the Mojave yucca bark, from which the following have been isolated so far: smilogenin, sarsapogenin, markogenin, samogenin, gloriogenin, convallamarogenin [40, 49], macranthogenin, schidegeragenin C, 5ß-spirost-25(27)-ene-3ß-ol-12-one [40], gitogenin and neogotogenin [77]. There are three types of furostanol glycosides in yucca that have been isolated so far which are in the lesser proportion (~6.8 %) to the total saponins in yucca [49, 57]: 3-O-β-d-glucopyranosyl-(1→2)-[β-d-xylopyranosyl-(1→3)]-β-d-glucopyranosyl-5β(25R)-furostan-3β,22α,26-triol 26-O-β-d-glucopyranoside, 3-O-β-d-glucopyranosyl-(1→2)-[β-d-xylopyranosyl-(1→3)]-β-d-glucopyranosyl-5β(25R)-furost-20(22)-en-3β,26-diol-12-one 26-O-β-d-glucopyranoside, and 3-O-β-d-glucopyranosyl-(1→2)-β-d-glucopyranosyl-5β(25R)-furostan-3β,22α,26-triol 26-O-β-d-glucopyranoside. Saponins form insoluble complexes with cholesterol, other sterols and bile acids and prevent their absorption in the intestine resulting in a decreased level of cholesterol in the blood of people and farm and laboratory animals [1, 3, 27, 28, 29, 57, 80]. Steroidal saponins have been found to have anti-proliferative [4] and phytoestrogenic [60] activity.

**Stilbenes—representation and roles**

Natural stilbenes are a group of phenolic phytochemicals with a characteristic 1,2-diphenylethylene nucleus [65]. Stilbenes found in yucca include: resveratrol, trans-3,3′,5,5′-tetrahydroxy-4′-methoxystilbene, larixinol, yuccaols A, B, C, D, E [4, 9, 37, 48, 49, 56] and yuccaone A [49, 57]. Natural polyphenols are secondary metabolites of plants produced for their own protection against stressful environmental conditions [58]. Phenolic compounds of yucca extracts have demonstrated antioxidant activity on the autoxidation of membrane lipids, especially of linoleic acid C18:2n-6 [22], which is the precursor of inflammatory 2-series prostaglandins (PG), such as PGE2 [12]. Stilbenes have been shown to inhibit NF-κB [9], the inducible transcription factor linked to inflammatory and immune responses, through the activation of cyclooxygenase 2 (COX-2) expression and the production of PGE2 [10, 61]. The synthesis of PGs and massive production of reactive oxygen species (ROS) is also linked with the ovulation of the dominant follicles on the ovary [63]. Resveratrol, yuccaols A and C, and trans-3,3′, 5,5′-tetrahydroxy-4′-methoxystilbene reduce excessive levels of reactive oxygen species (ROS), thus exhibiting strong protective activity against oxidative stress [48], that is inter alia, associated with carcinogenesis in several organs [26], including ovaries [33] and breasts [7] of women. The most studied biological effects and mechanisms of action are that of resveratrol particularly due to its high presence in some other plants with higher consumption by people, such as grapevines and their products. Resveratrol is known as a very promising antioxidant and anti-cancer compound and it has a perspective use in

**Table 1. Summary of *in vitro* and *in vivo* studies on the effect of *Yucca schidigera* on female reproduction**

| Animal species | Study | *Y. schidigera* dose | Effects | Reference |
|---|---|---|---|---|
| Cow | *in vivo* | | Increased conception rates | Cheeke, 2000 [8] |
| Pig | *in vivo* | 120 g yucca powder per tonne feed; 3 weeks prior to and 3 weeks after parturition | Reduction in stillbirths and pre-weaning mortality. | Herpin et al., 2004 [21] |
| Goat | *in vivo* | 250 and 500 mg yucca powder per head per day; 21 days pre-mating up to end of lactation | Shortening of oestrous cycle, increasing fertility rate and kidding rate. | Khalifa et al., 2014 [28] |
| Pig | *in vitro* | 1, 10 and 100 µg yucca extract cultured with ovarian granulosa cells | Inhibited T (at 1 and 10 µg) release, proliferation (PCNA), and promoted P4 release (at 100 µg) and apoptosis (bax). | Štochmaľová et al., 2014 [73] |
| Rabbit | *in vitro* | 1 µg yucca extract cultured with ovarian fragments | Stimulation of P4 release, no significant effect on T or E2 release. | Štochmaľová et al., 2015 [74] |
| Rabbit | *in vivo* | 5 or 20 g yucca powder per 100 kg feed; 50 days | Higher fecundity, conception rates and kindling rates as well as the blood levels of OT, P4, and PGF. | Štochmaľová et al., 2015 [74] |
| Sheep | *in vitro* | 1 and 100 µg yucca extract cultured with ovarian fragments | Stimulation of P4 release at 100 µg and inhibition of IGF-I release at 1 µg. No significant effect on T or E2 release. | Vlčková et al., 2017 [81] |
| Sheep | *in vivo* | 1.5 g yucca powder per head in diet; 30 days | Suppression of follicular growth, steroidogenesis (reduced serum P4 and E2), promotion of ovarian apoptosis (bax), and alteration of responsiveness of ovarian cells to FSH (reduced P4). No significant effect on T or IGF-I levels, responsiveness to FSH or cell proliferation. | Vlčková et al., 2017 [81] |
| Rabbit | *in vitro* | 0.1 % benzene cultured with ovarian fragments collected from does fed on diet supplemented with 5 or 20 g yucca powder per 100 kg feed for 350 days | Supplemental yucca reduced ovary resistance to benzene via inhibition of PGF release. | Földešiová et al., 2017 [15] |
| Rabbit | *in vivo* | 5 or 20 g yucca powder per 100 kg feed; 350 days | Increased conception rates and kindling rates as well as the blood levels of OT and PGF. Level of P4 in the blood was dose-dependent Stimulation of P4 and PGF release and reduction of IGF-I release, although no significant effect on OT release. | Földešiová et al., 2017 [15] |
| Mouse | *in vitro* | 10 µg yucca extract cultured with whole ovaries | Stimulation of P4 release in lean, normal and slightly obese mice. No significant effect on T or IGF-I release or on obese mice. | Sirotkin et al. 2017 [71] |
| Quail | *in vivo* | 100 or 200 mg per kg lead diet; 6 weeks | Increase in fertility rate and hatchability rate. | Alagawany et al., 2018 [2] |
| Horse | *in vitro* | 1, 10, 100 µg yucca extract cultured with ovarian fragments | Stimulation of P4 release at each dose compared to control although with gradual decreasing tendency at doses 10 and 100 µg | Vlčková, Sopková, Valocký (unpublished data) |

E2 — oestradiol-17ß; FSH — follicle-stimulating hormone; IGF-I — insulin-like growth factor; OT — oxytocin
P4 — progesterone; PCNA — proliferating cell nuclear antigen; PGF — prostaglandin F; T — testosterone

the prevention and reversal of many civilized diseases. Resveratrol induces intranuclear accumulation of COX-2 and facilitates p53-dependent and p53-independent apoptosis of cancer cells [33] as well as induces caspase 3 and up-regulates bax levels [18]. Since studies on its pro-apoptotic properties in normal ovarian cells are contradictory [35, 36, 41, 50], the mechanism is still not clearly explained yet. The inhibitory influence of resveratrol on the proliferation of ovarian cells has been demonstrated [50]. In addition, resveratrol was shown: to affect transcriptional activity of estrogen receptors (ER) [6], to have limited anti-oestrogenic activity [42], to reduce the levels of plasma IGF-I [13], to promote expression of genes encoding the LH receptors [41], steroidogenic enzymes and P4 production [31]; however, some studies opposed to anti-steroidogenic properties of resveratrol have been found [50].

### Effects of *Y. schidigera* on THE reproductive performance of females and THE morphology of THE reproductive organs

The dietary supplemental yucca increased conception rates in cattle [8], dairy goats [28], and rabbit does [74]. Yucca contains high levels of calcium and after ingestion, it can decrease the plasma levels of urea [8, 28], shorten the oestrous cycle, and increase the fertility rate and kidding rate in goats [28]. H e r p i n et al. [21] observed the positive effect of the application of Mojave yucca powder on pregnant sows for 3 weeks prior to parturition and 3 weeks after parturition by the reduction of stillbirths and pre-weaning mortality with an improvement of the overall health in piglets. Fifty-day feeding of a diet enriched with yucca powder positively influenced the kindling rate in rabbit does with no significant effect on the number of live born, stillborn or weaned pups per doe [15, 73]. A l a g a w a n y et al. [2] observed the improvement in fertility and hatchability percentage in Japanese quails fed a lead diet supplemented with *Yucca schidigera* extract.

Regarding the yucca influence on reproductive organs morphology, there are few research articles available. In our previous study in ewes [81], yucca powder feeding for 30 days reduced ovarian folliculogenesis in the early antral follicle stage by reducing the size of these follicles; although it had no significant effect on the size or number of larger follicles and therefore the size or weight of the ovaries. The weight and length of oviducts were also unaffected.

## PHYSIOLOGICAL ACTION OF OVARIAN AND GONADOTROPIC HORMMONES

The key regulators of ovarian activity are female steroid (progesterone, P4; oestradiol-17ß, E2) and peptide (insulin-like growth factor I, IGF-I) hormones [20, 66], which play important roles in the growth and differentiation of reproductive tissue and in the maintenance of fertility [11, 20]. Cholesterol is a substrate for the production of steroid hormones de novo. All steroid hormones signal via nuclear receptors to regulate transcriptional events [11].

Progesterone is a hormone with a key role in ovulation, luteinisation, implantation and the maintenance of pregnancy [11, 19], even though it also has a great importance in the induction of ovarian steroidogenesis, suppression of apoptosis in ovarian cells [66, 68], and together with IGF-I, promotes granulosa cells proliferation [64, 68, 82]. Progesterone receptors can be detected on theca cells of small antral follicles and the granulosa cells of preovulatory follicles exposed to LH surge [45], thus strongly regulating the process of ovulation [30].

Androgens (androstenedione and testosterone) act via androgen receptors on granulosa, stromal, and theca cells and oocytes of rat, pig and mice [16, 17]. On one hand, androgens have been reported to enhance granulosa cells proliferation, promote the growth of follicles in the early stages of folliculogenesis, promote steroidogenesis, and maturation of oocyte [11, 16]. However, on the other hand, androgens prevent the development of the follicles by stimulating apoptosis and atresia [11, 66]. Androgen receptor activation increases IGF-I and its receptor gene expression in the granulosa and theca cells of growing follicles and in the oocytes of primordial follicles [16].

Oestrogens are essential for folliculogenesis beyond the antral stage depending on the action of follicle stimulating hormone (FSH) and are necessary for maintaining the female phenotype of ovarian somatic cells [11]. Oestrogens signal via two forms of oestrogen receptors, α and ß, where in the ovary the latter is predominant [53, 55] and is essential for the follicle development and maturation [11].

The production of steroids in the ovaries depends on the cooperation between granulosa and theca cells (classical two-cell-two-gonadotropins model of steroidogenesis) [11, 66] accumulating in the follicular fluid. This allows steroids to act as paracrine factors, although various

amounts enter the systemic circulation and actively participate in the regulation of pituitary gonadotropins (FSH and LH) secretion [11].

FSH has an important role in the promotion of folliculogenesis through the stimulation of the growth of antral follicle/s to the pre-ovulatory stage, oocyte maturation, and the formation of LH receptors (in that follicle/s enabling LH to proceed to ovulation in the most sensitive follicle/s, luteinisation and formation of corpus luteum/corpora lutea) [39, 51]. FSH also positively influences the proliferation of ovarian cells [69], probably through the positive action on IGF-I production [68], which reduces the apoptosis of ovarian cells [25], and promotes the release of steroid hormones [25, 68].

In contrast to FSH, LH stops the proliferation of ovarian cells and induces their resistance to apoptosis via the induction of P4 receptors formation [59]. In cultured ovarian cells LH addition to the medium stimulated P4, E2, and IGF-I [68, 70].

IGF-I, a peptide hormone produced, inter alia, in the ovaries, is known to have stimulatory effects on folliculogenesis via stimulatory (proliferation of granulosa cells, follicular steroidogenesis, control of ovulation) and inhibitory (apoptosis of granulosa cells) actions [38, 39, 64, 68, 82]. It also can augment the expression of both FSH and LH receptors and the response of ovarian cells [44] and oocytes [54] to gonadotropins. All these physiological actions of hormones can be modulated by the use of medicinal plants, their extracts or active substances *in vivo* and *in vitro*; although the mechanisms of possible modulatory pathways remain unclear and require further studies for elucidation.

**Effects of *Y. schidigera* on the release of ovarian hormones and their response to upstream hormonal regulators**

Fifty-day dietary enrichment with yucca powder increased the levels of oxytocin (OT) and prostaglandin (PG) F in the plasma of rabbit does [15, 73] as well as P4 whose level depended on a dose of yucca fed to these animals or added to the culture medium. However, the change of OT release was not proven in *in vitro* experiments on rabbit ovarian fragments [15]. On the contrary, a thirty-day diet supplementation with yucca powder decreased the serum levels of P4 and E2 in ewes in late luteal phase of the oestrous cycle, but did not affect the levels of testosterone (T) and IGF-I; however, yucca promoted the release of IGF-I when responding to FSH added in the culture medium [81].

Yucca consumption have shown a significant hypocholesterolaemic effect in humans [27, 29], poultry [3], goats [28] and sheep [1, 80] that may relate to the reduction of substrate for the production of steroid hormones resulting in the suppression of P4 release by the ovaries [81].

It was found that yucca directly stimulated the release of P4 by porcine [73], rabbit [74], ovine [81], and murine [71] ovaries. The release of T was inhibited by yucca addition to cultured porcine granulosa cells [73], although it was not altered when added to rabbit [74] and ovine [81] ovarian fragments or mouse ovaries [71]. The E2 output by ovarian fragments of rabbits [74] and sheep [81] was not influenced markedly. The release of IGF-I by rabbit [15] or ovine [81] ovaries was inhibited, although not affected in mice ovaries [71]. This contradictory research shows that there could be species-specific actions of yucca on ovarian steroidogenesis and that these effects are dose-dependent (Table 1).

**Effects of *Y. schidigera* on proliferation and apoptosis of ovarian cells**

The influence of yucca on cell proliferation and apoptosis of ovarian cells *in vitro* and *in vivo* has been documented. *In vitro* studies reported a direct anti-proliferative and pro-apoptotic effect of yucca extract on cultured porcine granulosa cells through the reduced expression of PCNA and enhanced expression of bax, respectively [73]. The pro-apoptotic effect was also observed after a 30-day feed supplementation in ewes, whose granulosa cells contained high proportion of bax antigens, although no effect was proven on the proliferation of granulosa cells [81]. Since the findings on the proliferation of granulosa cells are inconsistent in these two animal models, additional experiments will be required.

**Phytoestrogenic and nonestrogenic effects of yucca constituents**

Stilbenes and steroidal saponins of yucca have shown mainly antioxidant properties [9, 10, 48] (which can affect folliculogenesis and steroidogenesis as reported in the studies using different plant additives [24, 75, 76]. Saponins are involved in the reduction of blood cholesterol, the substrate for steroidogenesis, and stilbenes can affect transcriptional activity of ERs [6]. Both the steroidal saponins and stilbenes have been shown to have phytoestrogenic activity by mimicking endogenous oestradiol-17β due to the fact they

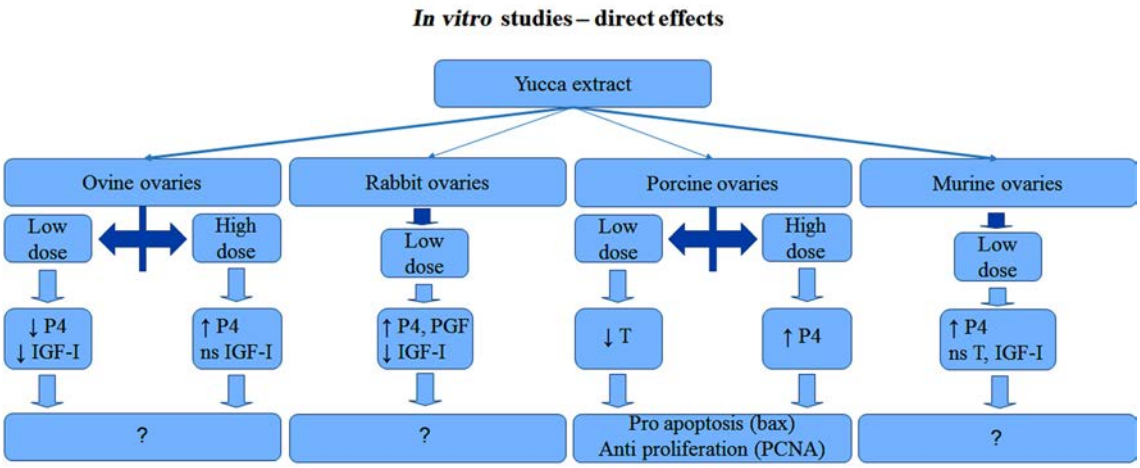


**Fig. 1. Direct effects of yucca extract on ovine, rabbit, porcine, and murine ovaries**
E2—oestradiol-17ß; FSH—follicle-stimulating hormone; IGF-I—insulin-like growth factor; OT—oxytocin; P4—progesterone
PCNA—proliferating cell nuclear antigen; PGF—prostaglandin F; T—testosterone; ↑—increase; ↓—decrease; ns—non-significant effect

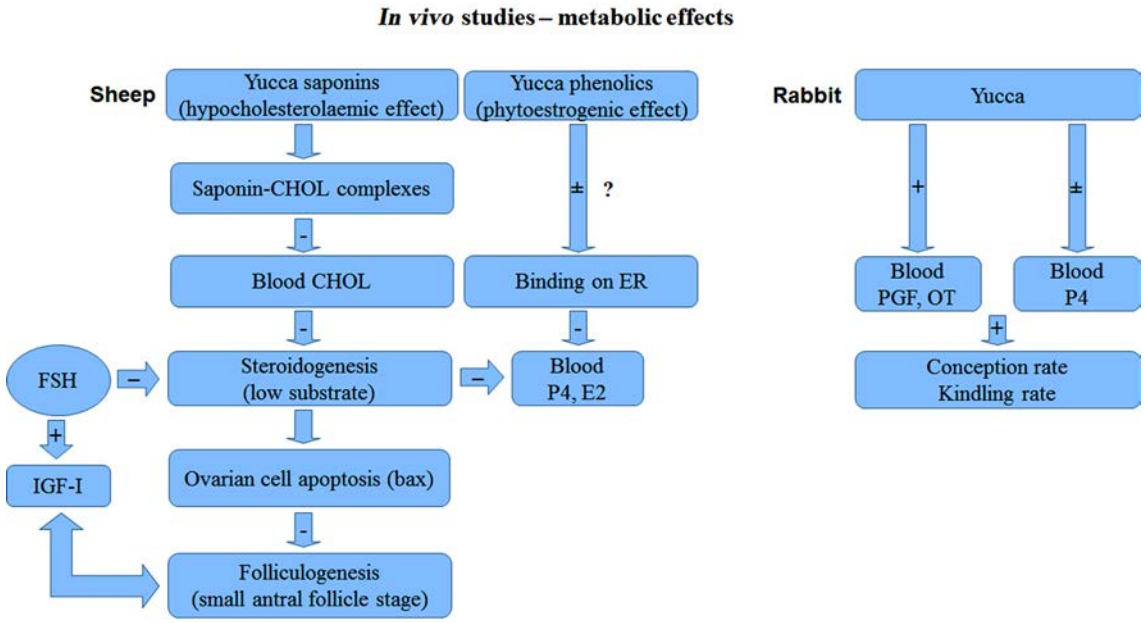


**Fig. 2. Supplemental yucca effects in sheep and rabbit does**
CHOL—cholesterol; E2—oestradiol-17ß; FSH—follicle-stimulating hormone; IGF-I—insulin-like growth factor
OT— oxytocin; P4—progesterone; PGF—prostaglandin F; ER—estrogen receptors

have similar chemical structure and can bind to ERα and ERβ [53, 60, 67, 84]. Phytoestrogens can competitively inhibit the production of oestradiol by aromatase [62] resulting in lower levels of endogenous oestrogen [23]. Besides this oestradiol-modulatory properties, phytoestrogens can moreover act via nonestrogenic mechanisms — directly activate intracellular regulators of the cell cycle and apoptosis, including IGF-I receptors [5] and mitogen-activated protein kinase (MAPK; ERK1/2) signal transduction cascade [5, 34, 83]. Such properties predetermine yucca to be the promising plant used in the prevention or therapy of various hormone-dependent diseases.

## CONCLUSIONS

The effects of Mojave yucca (*Y. schidigera*) researched *in vitro* and *in vivo* on several animal models have been reviewed. Yucca contains biologically active substances such as steroidal saponins and stilbenes that can influence

reproductive functions via oestrogenic and nonestrogenic mechanisms. However, these effects seem to be species-specific and dose-dependent. *In vitro* studies (Fig. 1) revealed the positive effect of yucca extract administration on the release of P4 by ovine, rabbit, porcine, and murine ovarian cells, however this direct effect depended on the dose of yucca added to the culture medium in ovine and pig ovarian fragments. Activation of these mechanisms or pathways results in initiation of bax-dependent apoptosis in ovarian cells (probably via blockage of cell proliferation through IGF-I receptors). On the one hand, *in vivo* studies (Fig. 2) performed in rabbit does, cows, goats, and quails showed a positive effect of supplemental yucca on reproductive performance, steroidogenesis and the production of PGF and OT; but on the other hand, yucca administration in sheep negatively influenced the development of small antral follicles and steroidogenesis. Due to the wide use of yucca in livestock breeding programs of farm animals and its use in the food industry, all of these effects of yucca on reproduction should be taken into account. Therefore, yucca actions on females require further studies aimed at the elucidation of the possible mechanisms of action in various animal models and women.

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## REFERENCES

1. **Aazami, M. H., Tahmasbi, A. M., Ghaffari, M. H., Naserian, A. A., Valizadeh, R., Ghaffari, A. H., 2013:** Effects of saponins on rumen fermentation, nutrients digestibility, performance, and plasma metabolites in sheep and goat kids. A*nn. Rev. Res. Biol.*, 4, 177—190.
2. **Alagawany, M., Abd El-Hack, M., Farag, M. R., Elnesr, S. S., El-Kholy, M. S., Saadeldin, I. M., Swelum, A. A., 2018:** Dietary supplementation of *Yucca schidigera* extract enhances productive and reproductive performances, blood profile, immune function, and antioxidant status in laying Japanese quails exposed to lead in the diet. *Poultry Science*, 97, 3126—3137.
3. **Aslan, R., Dundar, Y., Eryavuz, A., Bulbul, A., Kuçukkurt, I., Fidan, A. F., et al., 2005:** Effects of various quantities of *Yucca schidigera* powder (*Deodorase*) added to diets on the performance, some haematological and biochemical blood parameters, and total antioxidant capacity of laying hens. *Revue Méd. Vét.*, 156, 350—355.
4. **Balestrieri, C., Felice, F., Piacente, S., Pizza, C., Montoro, P., Oleszek, W., Visciano, V., Balestrieri, M. L., 2006:** Relative effects of phenolic constituents from *Yucca schidigera* Roezl. bark on Kaposi's sarcoma cell proliferation, migration, and PAF synthesis. *Biochem. Pharmacol.*, 71, 1479—1487.
5. **Bourque, M., Dluzen, D. E., Di Paolo, T., 2012:** Signalling pathway mediating the neuroprotective effects of sex steroids and SERMs in Parkinson's disease. F*ront. Neuroendocrinol.*, 33, 169—178.
6. **Bowers, J. L., Tyulmenkov, V. V., Jernigan, S. C., Klinge, C. M., 2000:** Resveratrol acts as a mixed agonist/antagonist for estrogen receptors alpha and beta. *Endocrinology*, 141, 3657—3667.
7. **Chatterjee, A., Ronghe, A., Singh, B., Bhat, N. K., Chen, J., Bhat, H. K., 2014:** Natural antioxidants exhibit chemopreventative characteristics through the regulation of CNC b-Zip transcription factors in estrogen-induced breast carcinogenesis. *J. Biochem. Mol. Toxicol.*, 28, 529—538.
8. **Cheeke, P. R., 2000:** Actual potential applications of *Yucca schidigera* and *Quillaja saponaria saponins* in human and animal nutrition. *Proc. Phytochem. Soc. Eur.*, 45, 241—254.
9. **Cheeke, P. R., Piacente, S., Oleszek, W., 2006:** Anti-inflammatory and anti-arthritic effects of *Yucca schidigera.* J. *Inflamm.*, 3, 6.
10. **Cianciulli, A., Calvello, R., Cavallo, P., Dragone, T., Carofiglio, V., Panaro, M. A., 2012:** Modulation of NF-κB activation by resveratrol in LPS treated human intestinal cells results in downregulation of PGE2 production and COX-2 expression. *Toxicol. In Vitro*, 26, 1122—1128.
11. **Drummond, A. E., 2006:** The role of steroids in follicular growth. *Reprod. Biol. Endocrinol.*, 4, 16—27.
12. **Eilati, E., Bahr, J. M., Hales, D. B., 2013:** Long term consumption of flaxseed enriched diet decreased ovarian cancer incidence and prostaglandin E2 in hens. *Gynecol. Oncol.*, 130(3), 620—628.
13. **Ergenoglu, M., Yildirim, N., Yildirim, A. G., Yeniel, O., Erbas, O., Yavasoglu, Taskiran, D., Karadadas, N., 2015:** Effects of resveratrol on ovarian morphology, plasma anti-Mullerian hormone, IGF-I levels, and oxidative stress parameters in a rat model of polycystic ovary syndrome. *Reprod. Sci.*, 22, 942—947.
14. **Fidan, A. F., Dündar, Y. J., 2008:** The effects of *Yucca schidi-*

*gera* and *Quillaja saponaria* on DNA damage, protein oxidation, lipid peroxidation, and some biochemical parameters in streptozotocin-induced diabetic rats. *J. Diabetes Complic.*, 22, 348—356.

15. **Földešiová, M., Baláži, A., Chrastinová, Ľ., Pivko, J., Kotwica, J., Harrath, A. H., et al., 2017:** *Yucca schidigera* can promote rabbit growth, fecundity, affect the release of hormones *in vivo* and *in vitro*, induce pathological changes in liver, and reduce ovarian resistance to benzene. *Anim. Reprod. Sci.*, 183, 66—76.
16. **Gervásio, C. G., Bernuci, M. P., Silva-de-Sá, M. P., Japur de Sá Rosa-e-Silva, A. C., 2014:** The role of androgen hormones in early follicular development. I*SRN Obstetrics and Gynecology, eCollection 2014*; 818010, 11 pp.
17. **Gill, A., Jamnonjgit, M., Hammes, S. R., 2004:** Androgens promote maturation and signalling in mouse oocytes independent of transcription: a release of inhibition model for mammalian oocyte meiosis. *Mol. Endocrinol.*, 18, 97—104.
18. **Gokbulut, A. A., Apohan, E., Baran, Y., 2013:** Resveratrol and quercetin-induced apoptosis of human 232B4 chronic lymphocytic leukemia cells by activation of caspase-3 and cell cycle arrest. *Hematology*, 18, 144—150.
19. **Hagan, C. R., Faivre, E. J., Lange, C. A., 2009:** Scaffolding actions of membrane-associated progesterone receptors. *Steroids*, 74, 568—572.
20. **Hernandez-Medrano, J., Campbell, B. K., Webb, R., 2012:** Nutritional influences on folliculogenesis. *Reprod. Domest. Anim.*, 47 (Suppl. 4), 274—282.
21. **Herpin, P., Vincent, A., Cheeke, P. R., 2004:** Effect of feeding *Yucca schidigera* (DK powder) to the sow on piglet blood oxygenation and survival. *Proc. West Sect. Am. Soc. An. Sci.,* 55, 145—150.
22. **Igile, G., Oleszek, W., Jurzysta, M., Burda, S., Fafunso, M., Fasanmade, A. A., 1994:** Flavonoids from Vernonia amugdalina and their antioxidant activities. *J. Agric. Food Chem.*, 42, 2445—2448.
23. **Jefferson, W. N., Patisaul, H. B., Williams, C. J., 2012:** Reproductive consequences of developmental phytoestrogen exposure. *Reproduction*, 143, 247—260.
24. **Jha, U., Asad, M., Asdaq, B. M. S., Das, K. A., Satya, P. S. V., 2010:** Fertility inducing effect of aerial parts of *Coccinia cordifolia* L. in female rats. *J. Ethnopharmacol.*, 127, 561—564.
25. **Jiang, Y., Cheung, C. K. M., Wang, Y., Tsang, B. K., 2003:** Regulation of cell death and cell survival gene expression during ovarian follicular development and atresia. *Front. Biosci.*, 8, d222—237.
26. **Kang, N. J., Shin, S. H., Lee, H. J., Lee, K. W., 2011:** Polyphenols as small molecular inhibitors of signalling cascades in carcinogenesis. *Pharmacol. Therapeut.*, 130, 310—324.
27. **Kemertelidze, É. P., Benidze, M. M., Skhirtladze, A. V., 2009:** Steroid compounds from *Yucca gloriosa* L. introduced into Georgia and their applications. *Pharma. Chem. J.*, 43, 45*gloriosa*47.
28. **Khalifa, E. I., Hanan, A. M. H., Mohamed, A. H., Hussein, A. M., 2014:** Effects of using *Yucca schidigera* powder as feed additive on productive and reproductive efficiency of Zaraibi dairy goats. *Egypt J. Sheep Goat Sci.*, 9, 9—21.
29. **Kim, S. W., Park, S. K., Kang, S., Kang, H. C., Oh, H. J., Bac, C. Y., Bac, D. H., 2003:** Hypocholesterolemic property of *Yucca schidigera* and *Quillaia saponaria* extracts in human body. *Arch. Pharm. Res.*, 26, 1042—1046.
30. **Kim, J., Bagchi, I. C., Bagchi, M. K., 2009:** Control of ovulation in mice by progesterone receptor-regulated gene networks. *Mol. Hum. Reprod.*, 15, 821—828.
31. **Kolesarova, A., Capcarova, M., Maruniakova, N., Lukac, N., Ciereszko, R. E., Sirotkin, A. V., 2012:** Resveratrol inhibits reproductive toxicity induced by deoxynivalenol. *J. Environ. Sci. Health A. Tox. Hazard. Subst. Environ. Eng.*, 47, 1329—1334.
32. **Kowalczyk, M., Pecio, Ł., Stochmal, A., Oleszek, W., 2011:** Qualitative and quantitative analysis of steroidal saponins in crude extract and bark powder of *Yucca schidigera* Roezl. *J. Agric. Food Chem.*, 59, 8058—8064.
33. **Lin, C., Crawford, D. R., Lin, S., Hwang, J., Sebuyira, A., Meng, R., et al., 2011:** Inducible COX-2-dependent apoptosis in human ovarian cancer cells. *Carcinogenesis*, 32, 19—26.
34. **Lin, H. Y., Lansing, F. B., Merillon, J. M., Davis, F. B., Tang, H. Y., Shih, A., et al., 2005:** Integrin αVß3 contains a receptor site for resveratrol. *FASEB J.*, 20, 1742—1744.
35. **Liu, M., Yin, Y., Ye, X., Zeng, M., Zhao, Q., Keefe, D. L., Liu, L., 2013:** Resveratrol protects against age-associated infertility in mice. *Hum. Reprod.*, 28, 707—717.
36. **Macedo, T. J. S., Barros, V. R. P., Monte, A. P. O., Gouveia, B. B., Bezerra, M. É. S., Cavalcante, A. Y. P., et al., 2017:** Resveratrol has dose-dependent effects on DNA fragmentation and mitochondrial activity of ovine secondary follicles cultured *in vitro*. *Zygote*, 11, 1—9.
37. **Marzocco, S., Piacente, S., Pizza, C., Oleszek, W., Stochmal, A., Pinto, A., Sorrentino, R., Autore, G., 2004:** Inhibition of inducible nitric oxide synthase expression by yuccaol C from *Yucca schidigera* Roezl. *Life Sci.*, 75, 1491—1501.
38. **Mazerbourg, S., Bondy, C. A., Zhou, J., Monget, P., 2003:** The insulin-like growth factor system: a key determinant role

in the growth and selection of ovarian follicles? A comparative species study. *Reprod. Domest. Anim.*, 38, 247—258.

39. **Mihm, M., Evans, A. C., 2008:** Mechanisms for dominant follicle selection in monovulatory species: a comparison of morphological, endocrine and intraovarian events in cows, mares and women. *Reprod. Domest. Anim.*, 43 (Suppl. 2), 48—56.
40. **Miyakoshi, M., Tamura, Y., Masuda, H., Mizutani, K., Tanaka, O., Ikeda, T., et al., 2000:** Antiyeast steroidal saponins from *Yucca schidigera* (*Mohave Yucca*), a new anti-food-deteriorating agent. J. *Nat. Prod.*, 63, 332.
41. **Morita, Y., Wada-Hiraike, O., Yano, T., Shirane, A., Hirano, M., Hiraike, H., et al., 2012:** Resveratrol promotes expression of SIRT1 and StAR in rat ovarian granulosa cells: An implicative role of SIRT1 in the ovary. *Reprod. Biol. Endocrinol.*, 10, 14.
42. **Mueller, S. O., Simon, S., Chae, K., Metzler, M., Korach, K. S., 2004:** Phytoestrogens and their human metabolites show distinct agonistic and antagonistic properties on estrogen receptor alpha (ERalpha) and ERbeta in human cells. *Toxicol. Sci.*, 80, 14—25.
43. **Narvaez, N., Wang, Y., McAllister, T., 2013:** Effects of extracts of Humulus lupulus (hops) and *Yucca schidigera* applied alone or in combination with monensin on rumen fermentation and microbial populations *in vitro*. *J. Sci. Food. Agric.*, 93, 2517—2522.
44. **Natesampillai, S., Veldhuis, J. D., 2004:** Involvement of Sp1 and SREBP-1a in transcriptional activation of the LDL receptor gene by insulin and LH in cultured porcine granulosa-luteal cells. *Am. J. Physiol. Endocrinol. Metab.*, 287, E128—E135.
45. **Natraj, U., Richards, J. S., 1993:** Hormonal regulation, localization, and functional activity of the progesterone receptor in granulosa cells of rat preovulatory follicles. *Endocrinology*, 133, 761—769.
46. **Olas, B., Wachiwicz, B., Saluk-Juszezak, J., Zielinski, T., Kaca, W., Buczynski, A., 2001:** Antioxidant activity of resveratrol in endotoxin-stimulated blood platelets. *Cell. Biol. Toxicol.*, 17, 117—125.
47. **Olas, B., Wachovicz, B., Stochmal, A., Oleszek, V., 2002:** Anti-platelet effects of different phenolic compounds from *Yucca schidigera* Roezl. bark. *Platelets*, 13, 167—173.
48. **Olas, B., Wachovicz, B., Stochmal, A., Oleszek, V., 2003:** Inhibition of oxidative stress in blood platelets by different phenolics from *Yucca schidigera* Roezl. bark. *Nutr.*, 19, 633—640.
49. **Oleszek, W., Sitek, M., Stochmal, A., Piacente, S., Pizza, C., Cheeke, P., 2001:** Steroidal saponins in *Yucca schidigera* Roezl. *J. Agric. Food. Chem.*, 49, 4392—4396.
50. **Ortega, I., Duleba, A. J., 2015:** Ovarian actions of resveratrol. *Ann. NY Acad. Sci.*, 1348, 86—96.
51. **Palermo, R., 2007:** Differential actions of FSH and LH during folliculogenesis. *Repris. Biomed. Online*, 15, 326—337.
52. **Patel, S., 2012:** Yucca: A medicinally significant genus with manifold therapeutic attributes. *Nat. Prod. Bioprospect.,* 2(6), 231—234.
53. **Paterni, I., Granchi, C., Katzenellenbogen, J. A., Minutolo, F., 2014:** Estrogen receptors alpha (ERα) and beta (ERß): subtype-selective ligands and clinical potential. *Steroids*, 90, 13—29.
54. **Patiño, R., Yoshizaki, G., Thomas, P., Kagawa, H., 2001:** Gonadotropic control of ovarian follicle maturation: the two-stage concept and its mechanisms. *Comp. Biochem. Physiol. B Biochem. Mol. Biol.*, 25, 198—207.
55. **Pelletier, G., Labrie, C., Labrie, F., 2000:** Localization of oestrogen receptor α, oestrogen receptor ß and androgen receptors in the rat reproductive organs. *J. Endocrinol.*, 165, 359—370.
56. **Piacente, S., Montoro, P., Oleszek, W., Pizza, C., 2004:** *Yucca schidigera* bark: Phenolic constituents and antioxidant activity. *J. Nat. Prod.*, 67, 882—885.
57. **Piacente, S., Pizza, C., Oleszek, W., 2005:** Saponins and phenolics of *Yucca schidigera* Roezl: Chemistry and bioactivity. *Phytochem. Rev.*, 4, 177—190.
58. **Quideau, S., Deffieux, D., Douat-Casassus, C., Pouységu, L., 2011:** Plant polyphenols: chemical properties, biological activities, and synthesis. *Angewandte Chemie—International Edition*, 50, 528—621.
59. **Quirk, S. M., Cowan, R. G., Harman, R. M., Hu, C. L., Porter, D. A., 2004:** Ovarian follicular growth and atresia: the relationship between cell proliferation and survival. *J. Anim. Sci.*, 82 (E-Suppl.), E40—E52.
60. **Rietjens, I. M., Sotoca, A. M., Vervoort, J., Louisse, J., 2013:** Mechanisms underlying the dualistic mode of action of major soy isoflavones in relation to cell proliferation and cancer risk. *Mol. Nutr. Food Res.*, 57, 100—113.
61. **Schwartz, J. I., Chan, C. C., Mukhopadhyay, S., McBride, K. J., Jones, T. M., Adcock, S., et al., 1999:** Selective inhibition of cyclooxygenase type-2 reverses endotoxin-induced fever in monkeys and naturally occurring fever in humans. *Clin. Pharmacol. Ther.*, 65, 653—660.
62. **Shanle, E. K. and Xu, W., 2011:** Endocrine disrupting chemicals targeting estrogen receptor signalling: identification and mechanisms of action. *Chem. Res. Toxicol.*, 24, 6—19.
63. **Shkolnik, K., Tadmor, A., Ben-Dor, S., Nevo, N., Galiani, D.,**

**Dekel, N., 2011:** Reactive oxygen species are indispensable in ovulation. *Proc. Natl. Acad. Sci. USA*, 108, 1462—1467.

64. **Silva, J. R., Figueiredo, J. R., van den Hurk, R., 2009:** Involvement of growth hormone (GH) and insulin-like growth factor (IGF) system in ovarian folliculogenesis. T*heriogenology*, 71, 1193—1208.
65. **Sirerol, J. A., Rodríguez, M. L., Mena, S., Asensi, M. A., Estrela, J. M., Ortega, A. L., 2016:** Role of natural stilbenes in the prevention of cancer. *Oxid. Med. Cell Longev.*, 2016; 3128951, 15 pp.
66. **Sirotkin, A. V., 2014:** *Regulators of Ovarian Functions*. 2nd edn., New York: Nova Science Publishers, Inc., 194 pp.
67. **Sirotkin, A. V., Harrath, A. H., 2014:** Phytoestrogens and their effects. *Eur. J. Pharmacol.*, 741, 230—236.
68. **Sirotkin, A. V., Makarevich, A. V., Grossmann, R., Kotwica, J., Schaeffer, H. J., Marnet, et al., 2003:** Regulators of ovarian functions. In **Luck, M. R. (Ed.):** *Regulation and Evaluation of Ovarian Function and Embryogenesis in Normal and Transgenic Animals in vitro and in vivo*. Research Institute of Animal Production, Nitra, Slovakia, 9–25.
69. **Sirotkin, A. V., Mlyncek, M., Makarevich, A. V., Florkovicova I., Hetenyi, L., 2008:** Leptin affects proliferation-, apoptosis- and protein kinase A-related peptides in human ovarian granulosa cells. *Physiol. Res.*, 57, 437—442.
70. **Sirotkin, A. V., Rafay, J., Kotwica, J., 2009:** Leptin controls rabbit ovarian function *in vivo* and *in vitro*: possible interrelationships with ghrelin. *Theriogenology*, 72, 765—772.
71. **Sirotkin, A. V., Fabian, D., Babeľová (Kubandová), J., Vlčková, R., Alwasel, S., Harrath, A. H., 2017:** Metabolic state can define the ovarian response to environmental contaminants and medicinal plants. *Appl. Physiol. Nutr. Metab.*, 42, 1264—1269.
72. **Sucharzewska, D., Stochmal, A., Oleszek, W., 2003:** The effect of *Yucca schidigera* extract on the physical structure and on the oxidative stability of sugar-candy foam products. *Food Sci. Technol.*, 36, 347—351.
73. **Štochmaľová, A., Kádasi, A., Alexa, R., Grossmann, R., Sirotkin, A. V., 2014:** The effect of Yucca on proliferation, apoptosis and steroidogenesis on porcine granulosa cells. *Potravinárstvo*, 8, 87—91.
74. **Štochmaľová, A., Földešiová, M., Baláži, A., Kádasi, A., Grossmann, R., Alexa, R., et al., 2015:** *Yucca schidigera* extract can promote rabbit fecundity and ovarian progesterone release. *Theriogenology*, 84, 634—638.
75. **Telefo, P. B., Moundipa, P. F., Tchana, A. F., Tchouanguep, D. C., Mbiapo, F. T., 1998:** Effects of aqueous extract of *Aloe buettneri, Dicliptera verticillata, Hibiscus macranthus,* and *Justicia insularis* on some biochemical and physiological parameters of reproduction in immature female rat. *J. Ethnopharmacol.*, 63, 193—200.
76. **Telefo P. B., Moundipa, P. F., Tchouanguep, F. M., 2004:** Inductive effects of the leaf mixture extract of *Aloe buettneri, Justicia insularis, Dicliptera verticillata,* and *Hibiscus macranthus* on *in vitro* production of estradiol. *J. Ethnopharmacol.*, 90, 225—230.
77. **Tenon, M., Feuillère, N., Roller, M., Birtić, S., 2017:** Rapid, cost-effective and accurate quantification of *Yucca schidigera* Roezl. steroidal saponins using HPLC-ELSD method. *Food Chem.*, 221, 1245—1252.
78. **Torres, P., Avila, J. G., de Vivar, A. R., Gacía, A. M., Marín, J. C., Aranda, E., Céspedes, C. L., 2003:** Antioxidant and insect growth regulatory activities of stilbenes and extracts from *Yucca periculosa. Phytochem.*, 64, 463—473.
79. **Uenobe, F., Nakamura, S., Miyazawa, M., 1997:** Antimutagenic effect of resveratrol against Trp-P-1. *Mutat. Res.,* 373, 197—200.
80. **Vlčková, R., Andrejčáková, Z., Sopková, D., 2015:** Effect of yucca powder feed supplementation on blood metabolic parameters of sheep. In *Physiology and Biochemistry in Animal Nutrition, Proceedings of the XIIth International Conference of Young Researchers*, 23—24 September, Lowicz-Nieborów, Poland, 61.
81. **Vlčková, R., Sopková, D., Andrejčáková, Z., Valocký, I., Kádasi, A., Harrath, et al., 2017:** Dietary supplementation of yucca (*Yucca schidigera*) affects ovine ovarian functions. *Theriogenology*, 88, 158—165.
82. **Webb, R., Campbell, B. K., 2007:** Development of the dominant follicle: mechanisms of selection and maintenance of oocyte quality. *Soc. Reprod. Fertil. Suppl.*, 64, 141—163.
83. **Yanagihara, N., Zhang, H., Toyohira, Y., Takahashi, K., Ueno, S., Tsutsui, M., Takahashi, K., 2014:** New insights into the pharmacological potential of plant flavonoids in the catecholamine system. *J. Pharmacol. Sci.*, 124,123—128.
84. **Younes, M., Hanna, N., 2011:** Estrogen receptor ß. *Arch. Pathol. Lab. Med.*, 135, 63—66.

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