



Protective Effects of Edible Plants against Nicotine Induced Reproductive Toxicity –A Review

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Article History:

Received on: 28 Sep 2019
Revised on: 21 Apr 2020
Accepted on: 20 May 2020

Keywords:

Nicotine,
Tobacco,
Male infertility,
Free Radicals,
Antioxidants,
Testosterone

ABSTRACT

Numerous examinations have announced that the Nicotine present in tobacco smoke adverse affects sperm parameters, fundamental plasma, and different other richness factors. These harms are because of the natural finding that smoking expands the degree of free radicals, consequently bringing about oxidative pressure. Accordingly, an increment of free radicals, DNA harm and lipid peroxidation in human sperm may happen to bring about impedance of sperm quality. Nicotine organization in trial creatures was initiated to influence spermatogenesis, epididymal sperm count, motility and treating capability of sperms. Huge quantities of restorative herbs have been recorded in Siddha framework that improve spermatogenesis and increment the nature of sperm. The present review gives an outline on the relationship between male richness incited by nicotine and defensive impacts of different natural plants on it. The paper additionally features the dynamic, common standards, and rough concentrates of plants, which have been valuable in improving nicotine instigated testicular harms and supportive in spermatogenesis and multiplication. Despite the fact that the discoveries of this survey propose numerous herbs are extremely viable against nicotine actuated male barrenness still increasingly clinical preliminaries are prescribed to show their viability on nicotine instigated male infertility.



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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i3.2606>

Production and Hosted by

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INTRODUCTION

In developing countries, Infertility is an understudied fear in sexual and reproductive health, until now its impact can be staggering. An incapability to conceive or bear children can outcome with important psychologic, economic, and medical implications. Environmental and lifestyle changes cause an adverse effect on fertility. Infertility is observed in 10 to 15% of the couples. The nature of human semen is breaking down in the southern division of India throughout the years, most likely because of ecological, dietary, way of life or finan-

cial causes (Singh *et al.*, 2010). Hormones aren't the fundamental issue in about 97% of sterile men. Barrenness in males has been with sperm dysfunctions, for example, low sperm count, adolescence, anomaly and absence of motility. In males, the impacts of smoking on androgen are significant.

Nicotine is a dynamic alkaloid, the popular significant segment in tobacco. Nicotine is a profoundly dangerous substance and it is consumed rapidly through the respiratory tract, oral mucosa and skin. Roughly 80 to 90% of nicotine is processed by the liver; however, the kidney and lungs are also included. Various examinations have demonstrated that utilization of nicotine contain mixes decline the sperm count and motility (Parandin *et al.*, 2012). An ongoing literature review broke down logical distributions on cigarette smoking and male infertility. The authors looked at 33 pertinent investigations of infertile smokers and found that: 30% of studies indicated decrease in sperm count 42% of studies demonstrated decrease in sperm morphology 40% of studies demonstrated decrease in sperm motility. Past examinations have shown that nicotine can harm sperm layer, DNA and initiate apoptosis in interstitial cells in testis. Anti-oxidant properties of natural plants, its impacts on conceptive hormones, epididymis pathway, and sperm include motility in nicotine-tainted rodents has not been researched. Numerous herbs are utilized in Siddha framework to improve the sperm quality and other treating characters of sperm. Plants and their concentrates wealthy in cell reinforcements assume a significant job in securing testicular harms brought about by nicotine.

Various plants have been talked about in detail. Some different plants just recorded in writing may likewise be of high logical significance. There is a need to lead pre clinical and clinical investigations to help customary cases and to work out cell and subatomic system associated with nicotine initiated barrenness. Nicotine, a pharmacologically dynamic alkaloid, is the most important part in tobacco (Mahdavi *et al.*, 2015). A few investigations have referenced that the initiation of Tobacco utilization takes puts in youngsters. This early beginning age implies that there is an open door for more introductions to the negative wellbeing impacts of Nicotine, which has harmful impacts, especially on the regenerative organs. Some impacts of nicotine on proliferation as significant increment in the frequency of barrenness rate in both human and research center animals (Asadi *et al.*, 2013). The survey is partitioned into a progression of segments, tending to the harms brought about by Nicotine on different conceptive tissues and their parameters, distinction in

portions, impacts of different plants in dealing with those harms.

Nicotine on reproductive tissue

Inside the body, nicotine is oxidized to its metabolite cotinine, which has a long half-life, and both the nicotine and the cotinine antagonistically influence spermatogenesis, epididymal sperm Count, motility, and the treating capability of sperms. Nicotine causes thickening of the tunica propria, brought about by an expansion in collagen strands under the sporadic basal lamina. It causes degeneration of Junctional specializations between the Sertoli cells (Vijayprasad *et al.*, 2014). Interminable organization of nicotine produce improved union of cholesterol, triglycerides, phospholipids and free unsaturated fats in the testicles. The movements of the lipogenic proteins stay unaltered in testicles. Nicotine causes oxidative pressure (OS) by meddling with the cancer prevention agent balance by expanding the creation of ROS. Nicotine can without much of a stretch go through the cell film and respond with tubulin protein present in the cytoplasm of duplicating cells, making issue cell.

Nicotine produces both reversible and irreversible harms in many tissues of the body in every single living creature and the degree of harm is species explicit and relies upon age, sexual orientation, hereditary foundation, and time of introduction and course of the organization. The oral organization of nicotine in rodents at a portion of 3.5 mg/kg body weight/day for the term of about a month is proportionate to the steady presentation to nicotine in smokers in people.

Nicotine dosage

Cigarette tobacco (containing approximately 2–3% nicotine) = 1–2 g per 100 g or 0.8–1.9 mg nicotine per tobacco rod. An average cigarette delivers roughly 10–30 $\mu\text{g kg}^{-1}$, typically resulting in 10–50 ng ml⁻¹ peak plasma levels (Chauhan *et al.*, 2014). In most of the studies, nicotine was administered intraperitoneally (Bhuvanewari and Elango, 2015). Whereas in some nicotine was administered intramuscularly. The studies of nicotine administered as nicotine tartrate was 0.1 mg/100 g BW, (Raji *et al.*, 2006), 0.25 mg/100g/day (Saeed *et al.*, 2015; Gambo *et al.*, 2013), 0.3mg/100g, 0.4mg/100g (Horak *et al.*, 2003), 0.5 mg/100g (Misra, 2009) and a dose of liquid nicotine was 0.5ml /kg (Mohammadghasemi and Jahromi, 2018) bodyweight of the animal.

Nicotine (free base) =162 g mole⁻¹ MW, whereas nicotine hydrogen tartrate=498 MW. In calculating the amount (mg) of the salt form needed to admin-

Table 1: List of plants that possess protective effects on nicotine induced reproductive toxicity taken for review

S.No	Plant Name/ Botanical Name	Family	Chemical/Properties
1.	Turmeric /Curcuma longa (Ozen <i>et al.</i> , 2002)	Zingiberaceae	Curcumin
2.	Eruca sativa (Asadi <i>et al.</i> , 2013)	Brassicaceae	Natural antioxidants such as polyphenols
3.	Nigella sativa (Ping <i>et al.</i> , 2014)	Ranunculaceae	Thymoquinone
4.	Coconut water, the liquid endosperm of coconut / Cocos nucifera	Arecaceae	Sugars, vitamins, minerals, proteins, free amino acids
5.	Urtica dioica (Parandin <i>et al.</i> , 2012)	Urticaceae.	Flavonoids.
6.	Chlophytum borivilianum (Adiga <i>et al.</i> , 2008)	Lilliaceae	Saponin and Flavonoides
7.	Zingiber officinale (Yousef <i>et al.</i> , 2003)	Zingiberaceae	Natural antioxidants Beta-carotene, Vitamin C, terpenoids, alkaloids, flavonoids and polyphenols
8.	Date palm /Phoenix Dactylifera (Bhuvaneswari and Elango, 2015)	Arecaceae	Natural antioxidants such as Phenolic present Gallic, ferulic, coumaric, caffeic acids and Flavonoides such as isoquercitrin, quercitrin, rutin, quercetin, and luteolin.
9.	Green Tea/Camellia sinensis Leaves (Saeed <i>et al.</i> , 2015)	Theaceae	Natural antioxidants such as Epigallocatechin Gallate, Epigallocatechin, Epicatechin Gallate and Epicatechin
10.	Saffron/ Crocus sativus	Iridaceae	Crocins, gallic acid, flavanoides, α -tocopherol

to achieve the desired free base nicotine dose, the following equation is useful (Tutka *et al.*, 2005) : [dose, mg/kg * BWt, kg * (nicotine salt form MW/nicotine free base MW)]/injection volume, ml.

Plants that prevent nicotine damages

Numerous plants have been analyzed for apply in Male infertility. There are just a couple of studies utilizing herbs and their concentrates to battle nicotine induced harmful consequences for spermatogenesis. A portion of those plants were assessed and recorded for future reference. Curcumin can be helpful in the treatment of male fruitlessness attributable to oligospermia and diminishing male sexual hormones. Eruca stimulate the procedure of spermatogenesis with a noteworthy ascent of sperm movement and increment in testosterone level to arrive at the typical qualities. It can invigorate the development of testicles and improve the expansion, development and separation of spermatozoa (Salahshoor *et al.*, 2016).

Regular antioxidants with free radical-scavenging movement, for example, polyphenols from green tea extricates have gotten a lot of consideration as potential, non-harmful, medications for oxidative pressure related neurotic conditions (Jalili *et al.*, 2014). Aqueous extract from the plant Chlophytum borivilianum brought about the enhancement of sexual brokenness, brought about improved sexual execution (Polis *et al.*, 2017). Date Palm pit decreases the damage delivered by Nicotine on testis and result in a noteworthy increment of testosterone level in serum of male, pale skinned person, rodents and increment spermatogenesis (Table 1).

Effects on sperm count and abnormal sperms

Johnsen criteria offer a helpful and quick technique for quantitative investigation of spermatogenesis. Nicotine (0.5 mL/kg) altogether diminished the motility, count and ordinary morphology of sperms gradual rise in portion of curcumin fun-

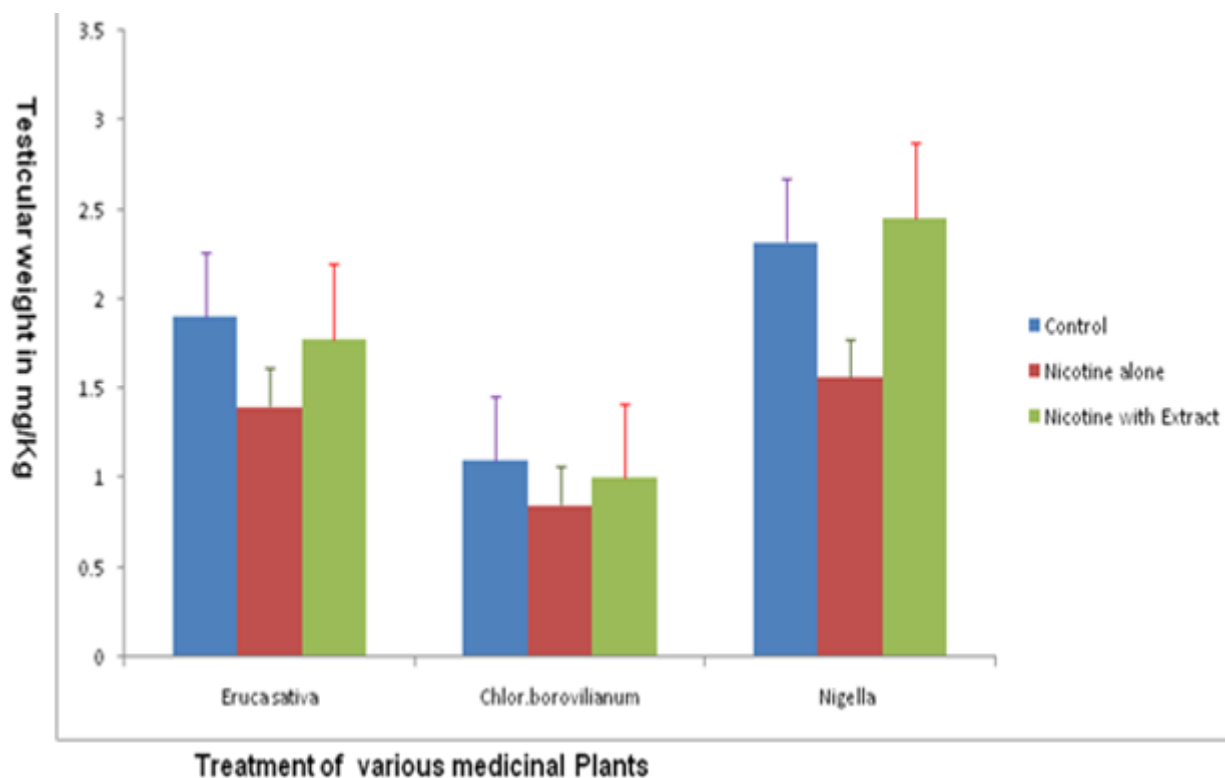


Figure 1: Efficacy of Nigella sativa, Chlorophytum borovilianum and Eruca sativa treatments against Nicotine induction on testicular weight

damentally prolonged the Sperm count and typical morphology of sperms in all gatherings. Delicate Coconut water and Mature Coconut water mixed treatment with nicotine demonstrated considerably higher epididymal sperm thickness, improvement in vas deferens weight and sperm include in examination with the nicotine treated control rats. Improved anomalies of sperm head are found in nicotine treated rodents, for example, turned body, separated head, irregular neck, round tail. The level of sperm was diminished on nicotine treatment. Coconut water supplementation considerably protected the sperms from the harming impact of nicotine and showed a decline in rate variation from the norm and improved dynamic development contrasted with nicotine treated rats. Mature coconut water additionally indicated that the sperm defensive impact by decreased variation from the norm and expanded pace of sperm development contrasted with nicotine treated rats (Kalpana *et al.*, 2007).

Eruca sativa seed oil demonstrated a huge improvement of all the testicular parameters of nicotine treated rodents. Eruca sativa seed oil was accounted to animate the procedure of spermatogenesis in rodents (Palani, 2018). Organization of Nigella sativa expanded the testicular cells count. At the same time, it decreased the harming impacts

brought about by nicotine on the testicular cells. The defensive impacts of Nigella sativa were showed by the solid, resistant reactivity of androgen receptor observed in the testicles, original vesicle and prostate organ of rodents. Nearness of dynamic compound thymoquinone could be the explanation behind the valuable impacts of Nigella sativa.

Green tea prevented the presence of barely any dispersed pyknotic cores in the basal cell layers. It likewise expanded the Interstitial Leydig cells. Zingiber officinale was exceptionally compelling in forestalling the nicotine instigated testicular harms by expanding the expert infertility possibilities in nicotine prompted male and furthermore female rodents. The plants that are wealthy in cancer prevention agents improve the sperm quality by expanding the declaration of cell reinforcement qualities in examination with nicotine influenced creatures.

Effects on morphometry and sperm motility

Testicular weight reduction is an important marker of gonadal toxicity. Administration of nicotine for at least 21 days showed a markable reduction in weight of testes. Nicotine (0.5 mL/kg) caused a significant decrease in the seminiferous tubules diameter in comparison with the control (ethanol-saline) group ($p < 0.05$) (Figure 1). The extracts of *Chlophytum borovilianum*, *Nigella sativa* and *Eruca sativa*

play a significant role in regulating seminiferous tubules diameter (Nair and Rajamohan, 2014).

As a result of Genotoxic effect of nicotine there is excess production of two highly mutagenic nitrosamine, *N'*-nitrosonor nicotine and 4-(methylnitrosamine)-1-(3-pyridyl)-1-butanone which product from nicotine during tobacco remedial or burning. Green tea improved the capacity of spermatozoa to penetrate oocytes. While the spermatogenic cells, owe to have an elevated level of unsaturated fatty acids, several dual links in the plasma membrane and low levels of cytoplasmic antioxidants, are sensitive to oxidative damage. Oxidation of the membrane fatty acids will result in the loss of membrane fluidity and will decrease the activity of enzymes and ion channels of sperm.

Effects on hormonal imbalance

Degeneration of the germ cells by nicotine cause a decrease in intratesticular convergences of testosterone, which is basic for the typical spermatogenesis just as for the support of the basic morphology and ordinary physiology of the seminiferous tubules. The plants listed here are rich in unsaturated fatty acids that stimulate the activity of 17 β -hydroxysteroid dehydrogenase, the most important key enzyme in the testosterone biosynthesis pathway (Aydos *et al.*, 2001). Crocin prevented the harm caused by nicotine on testosterone level. Nicotine caused a considerable reduce in spermatogenesis amount. Plants that increase Melatonin production can increase sperm chromatin integrity and improves spermatogenesis. All the plants listed in this review prevented the decrease in sperm quality and hormonal imbalances caused by nicotine. They significantly augmented serum testosterone concentration in nicotine administered animal models.

Among the biologically active compound in coconut water, L-arginine plays a main function in spermatogenesis. Seminal fluid is predominantly abundant in polyamines (putrescine, spermidine and spermine), polycationic products of L-arginine degradation, that are essential for cell growth and differentiation. Enhancing L-arginine provision may improve fertility in males by an enhanced synthesis of polyamines and L-arginine rich basic proteins in sperm cells. Nicotine and its metabolite cotinine have a direct cytotoxic effect on spermatozoa by damaging DNA. L-arginine also protects testicular tissue and preserves the spermatozoa against lipid peroxidation.

CONCLUSIONS

This review portrays the protective effects of various edible herbs and their extracts on nicotine induced on male rat reproductive toxicity in *In vivo* system. Though a number of evidences are available in the literature for plants used as aphrodisiacs and those increase sperm count and quality, Only a very few has been listed and proved scientifically, the mechanism in managing nicotine induced damages in testicular tissue. Efficacy of all other herbs and their extracts against nicotine induced infertility needs scientific updation. Various pathways involved must be taken into account to find a novel lead molecule of herbal origin to the treatment of nicotine induced sexual impairment. The medicinal plants mentioned in this study will promisingly improve the quality of sperm due to rich composition of natural antioxidants such as flavonoids. Thus the antioxidants help in scavenging the free radicals and to prevent lipid peroxidation within testes lead to enhancement of the testosterone levels and results in normal sperm counts.

Abbreviations

mg – milligram, ml – milliliter, kg – kilogram, gm – gram, bwt – Body weight, os – oxidative stress, Ros – reactive oxygen species.

ACKNOWLEDGEMENT

This is to thank R&D wing, Sree Balaji Medical College and Hospital and Dept of Anatomy, SBDCH, BIHER for their support and help in writing and completing this manuscript.

Conflict of Interest

There is no conflict between the authors.

Funding Support

No grant received from any funding agencies for this work.

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