

## Histological Effects of Ajwa on Oviduct after Nicotine Induced Toxicity in Adult Albino Rats

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### Abstract

**Introduction:** Nicotine changes histology of uterine tube and Ajwa stops nicotine from causing toxicity.

**Objectives:** To study the damages produced by nicotine in the oviduct of adult female albino rats and its protection by Ajwa fruit extract.

**Methods:** Three equal groups of 30 rats were made and maintained in the animal house of Punjab Postgraduate Medical Institute, Lahore. The control group A received no treatment except distilled water while among the two treated groups, group B received intraperitoneal nicotine injection (0.1 mg/kg body weight) for 28 days. The rats of group C were given 1000mg/kg body weight Ajwa fruit extract by gastric intubation plus 0.1mg/kg body weight intraperitoneal nicotine injection for 28 days.

**Results:** In nicotine treated rats of group B, mucosa of the fallopian tubes showed flattening of infoldings along with inflammatory cells and degenerated epithelial cells. Fibrosis and blood vessel congestion was present in serosa. Near normal restoration of oviduct structure was seen with Ajwa plus nicotine treated group C.

**Conclusion:** Nicotine can cause reversible injury to fallopian tubes and Ajwa improves oviduct histology, so it may be beneficial to recover sterility or subfertility caused by nicotine in women.

**Keywords:** Nicotine, Phoenix dactylifera, vascular congestion.

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### Introduction

Nicotine is present in many plants of family Solanaceae. Nicotine arrives in the human body as a part of tobacco smoke. 7 to 22 mg of nicotine is present in a cigarette.<sup>1</sup> In the United States, 35% men and 30% women of reproductive age are cigarette smokers.<sup>2</sup> In

a national report in united states, 24.2% women left smoking before becoming pregnant, 11% of women smoked in the 3 months before pregnancy and 75.8% of these women smoked during pregnancy.<sup>2</sup>

Extensive destructive effects of nicotine on fertility are recognizable. Moreover, there are notable damaging effects from passive/side-stream smoking. Female smokers withstand a four time greater threat of ectopic pregnancy than nonsmokers, and this connection is independent of other causative factors.<sup>3</sup> Female who smoked more than 20 cigarettes daily had an odd ratio (OR) of 3.5 for ectopic pregnancy relative to nonsmokers.<sup>4</sup>

Nicotine acts on nicotinic cholinergic receptors to ease neurotransmitter release (dopamine and others), producing happiness, excitement, mood adjustment.  $\alpha 4\beta 2$  receptor, predominant in human brain, mediates nicotine dependence.<sup>5</sup>

Nicotine causes degeneration of ovary and endometrium.<sup>6</sup> Smoking disrupts transport of the, sperm for

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fertilization, reproduction and embedding.<sup>7</sup> Nicotine administration affects sperm count and motility, reduces the spermatogenic cell line and causes anomalies of the sperm head.<sup>8</sup> A decrease in ciliary beat frequency is noted upon introduction of smoke solutions in hamster infundibulum, which is revocable upon washout of the smoke solution.<sup>9</sup> In rabbit, smoke inhalation affect electrical activity of oviduct.<sup>10</sup> Smoke inhalation momentarily effect patency of human Fallopian tube.<sup>11</sup>

Antioxidant property of the date palm increases reproductive function and fertility. Male flowers of Phoenix dactylifera L or date palm pollen can produce a suitable condition for oogenesis and maintain effective fecundity in female mice and is a useful nutraceutical for potentiation of fertility.<sup>12</sup> Gonad stimulating potency of Date palm pollen (DPP) have already confirmed by Egyptian scientists. Date palm pollen suspension contains cholesterol, carotenoids, rutin and estrone which increase FSH and LH and exhibit gonadotrophic activity.<sup>13</sup> Date extracts raise plasma levels of testosterone and estrogen, diameter of seminiferous tubules, increase sperm count, spermatogenesis and in male rats improve fertility.<sup>14</sup>

### Materials and Methods

Adult female albino rats were maintained at the Animal House of Punjab Postgraduate Medical Institute, Lahore. Rats were given a standard commercial diet, and water. Rats of each group were kept in separate cages. Rats were acclimatized for two weeks prior to experiment. Ajwa fruit extract was prepared by adding 1 liter distilled water to coarsely pounded date fruit (3:1). This was kept at 4°C with infrequent stirring.<sup>14</sup>

Group A were given distilled water by gastric intubation in addition to ordinary diet for 28 days. To group B, daily intraperitoneal injection of nicotine was given. To group C, each rat was given nicotine intraperitoneally and Ajwa fruit extract by gastric intubation for 28 days.

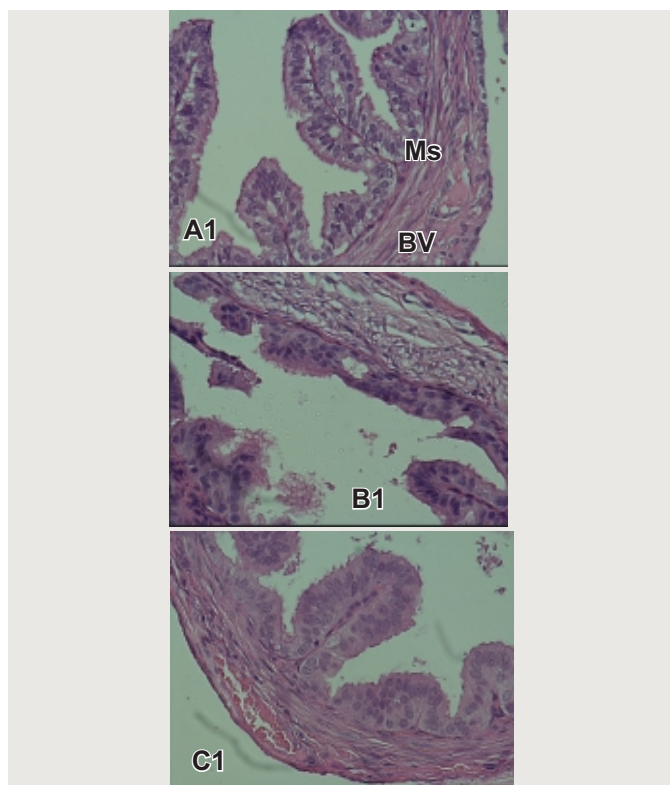
All animals were euthanized 48 hour after last dose and uterine tubes were removed, kept for 2 days in 10% neutral buffered formaldehyde solution. 5 µm thick sections of oviduct were cut, stained with Hematoxylin and Eosin and were watched under the light microscope. Comparison was made between group A, B and C. Masson Trichrome stained slides were observed for fibrosis.

Data was analyzed by using SPSS soft-ware package 20. Comparison among groups was performed by using ANOVA (one way). Tukey's test was used where necessary. P-value ≤0.05 was considered

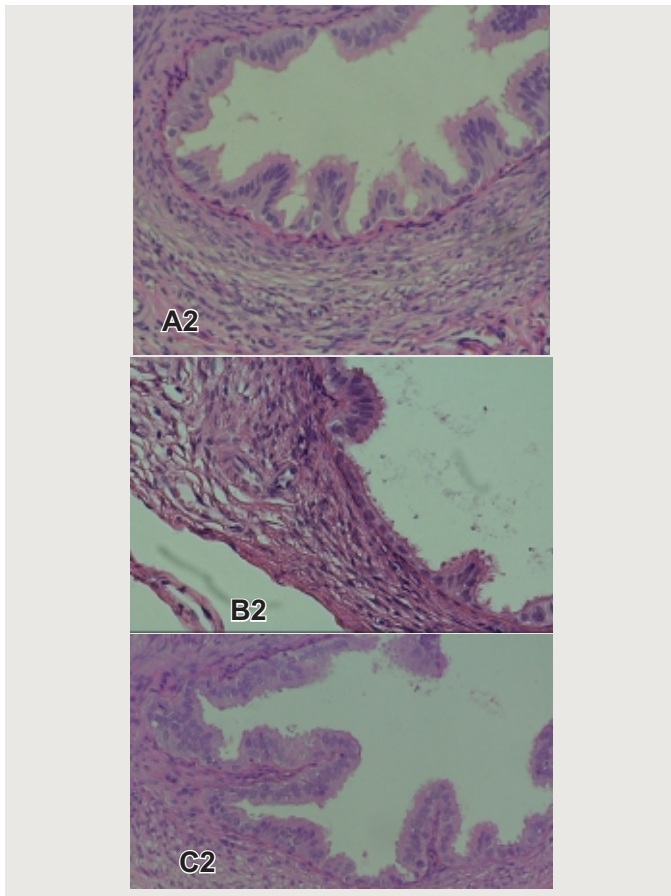
significant.

### Results

In group A, the oviduct showed folded mucosa each lined by ciliated columnar and non-ciliated secretory cells, surrounded by definite thick muscularis mucosae and serosa. (Fig. 1 & 2) All 10 animals of group B showed flattening of mucosal folds. Abundant degenerated epithelial cells and Inflammatory cells were present in mucosa, muscularis and serosa. Interstitial edema was seen with blood vessel congestion, and fibrosis in serosa (Fig. 1 & 2, Table 1 & 2). In group C, flattening of mucosal folds was present in 2 rats, degenerated epithelial cells, inflammatory cells infiltrate and interstitial edema reduced in outer layers. (Fig. 1 & 2)



**Figure 1:** Photomicrograph A1 of ampulla of oviduct of albino rat of control group A, showing well developed mucosal folds lined by ciliated and nonciliated columnar epithelium, muscularis (Ms) and serosa (S) with blood vessel in interstitial tissue. Photograph B1 shows decreased mucosal fold composed of less columnar cells with few cilia and more basal cells, edema and fibrosis (F) in serosa. In photomicrograph C1, folds are near normal with ciliated and nonciliated columnar epithelium, muscularis (Ms) and serosa (S) with congested blood vessels (CBV) in interstitial tissue. (10X, H & E)



**Figure 2.** A photomicrograph of isthmus of oviduct A2 of group A, showing well developed mucosal folds

lined by ciliated and nonciliated columnar epithelium. A photomicrograph of isthmus of fallopian tube B2 of group B, long black arrow showing more basal cuboidal cells and less no of columnar cells and straightening of mucosal folds. A photomicrograph of isthmus of fallopian tube C2 of group C, showing well developed mucosal folds lined by ciliated and nonciliated columnar epithelium near to control group. (40X, H & E)

## Discussion

In control group, tall mucosal folds, distinct muscularis mucosae and a thin serosa covered by mesothelium was present. Oviducts of rats of group B showed flattening of mucosal folds and inflammatory cell infiltration extended to the muscular and serosal layers. Degenerated epithelial cells were abundant. Edema was also present with blood vessel congestion and fibrosis in serosa. Increase in the formation of new collagen fibers dominate when recurrent injury occurs, and degradation of the already formed fibers decrease. Fibrosis occurs due to imbalance between fibrogenesis and fibrolysis. Inflammation and edema as effect of smoking on oviduct were also noted by Raieni<sup>15</sup> and there was no decrease in either the ciliated cells or the cilia.

Results of present study are partly in agreement with study performed by Morsy<sup>16</sup> on the fallopian tubes treated with methotrexate. Morsy noted blending and decline

**Table 1:** Distribution of Congestion of Blood Vessels among groups

Congestion of Blood Vessels	Ampulla				Isthmus			
	Group A n (%)	Group B n (%)	Group C n (%)	P value	Group A n (%)	Group B n (%)	Group C n (%)	P value
Absent	9 (90.0%)	0 (0.0%)	5 (50.0%)	.000**	10(100.0%)	0 (0.0%)	6(60.0%)	.000**
Present	1 (10.0%)	10 (100.0%)	5 (50.0%)	.000**	0 (0.0%)	10 (100.0%)	4(40.0%)	.000**

**Table 2:** Distribution of Fibrosis among groups

Fibrosis	Ampulla				Isthmus			
	Group A n (%)	Group B n (%)	Group C n (%)	P value	Group A n (%)	Group B n (%)	Group C n (%)	P value
Absent	10 (100.0%)	0 (0.0%)	6 (60.0%)	.000**	10 (100.0%)	0 (0.0%)	5 (50.0%)	.000**
Present	0 (0.0%)	10(100.0%)	4 (40.0%)	.000**	0 (0.0%)	10 (100.0%)	5 (50.0%)	.000**

**Table 3:** Distribution of Inflammatory cell infiltrate among groups

Inflammatory cell infiltrate	Ampulla				Isthmus			
	Group A n (%)	Group B n (%)	Group C n (%)	P value	Group A n (%)	Group B n (%)	Group C n (%)	P value
Absent	10 (100.0%)	0 (0.0%)	3 (30.0%)	.000**	10 (100.0%)	0 (0.0%)	5 (50.0%)	.000**
Present	0 (0.0%)	10 (100.0%)	7 (70.0%)	.000**	0 (0.0%)	10 (100.0%)	5 (50.0%)	.000**



in number of mucosal folds, inflammatory cells in mucosa and serosa, interstitial edema and blood vessel congestion in serosa. Eweka<sup>17</sup> noted disruption of the basement membrane, hemolysis in connective tissue cells, vacuolations and hypertrophied columnar epithelium in monosodium glutamate treated fallopian tubes.

Similarly, Sodium Fluoride treated oviduct showed some mononuclear cells infiltration, blood vessel congestion in an experiment by El-abd.<sup>18</sup> Similar results were noticed by Ghaly<sup>19</sup> where nicotine caused dilated and congested portal veins, degenerated hepatocytes and periportal inflammatory infiltration of mononuclear cells mainly lymphocytes. Increased prostaglandin synthesis due to nicotine toxicity caused dilated blood vessels by relaxation of smooth muscle and through releasing other vasodilator substances in blood.<sup>20</sup> The presence of infiltrating lymphocytes might be explained as a defense reaction in response to the nicotine toxicity.<sup>21</sup>

In 8 rats of group C, near normal mucosal folding, degenerated cells and inflammatory cells were less in number, thickened muscularis layer and blood vessel congestion was seen which was in agreement with the findings of Morsy<sup>16</sup> on oviduct when low dose methotrexate was given for longer period of time. Infiltration of inflammatory cells played a role in the reversible changes. Sodium fluoride decreased fibrosis in serosa in a study by El-abd.<sup>18</sup> Ajwa date extract (ADE) in combination with CCL422 decreased the area occupied by collagenous fibers. Similar results were noticed by Wahdan<sup>23</sup> when monosodium glutamate induced degenerative changes in oviduct were treated with vitamin C. Findings of Ali<sup>14</sup> were also in agreement with above study where ochratoxin induced tubular damage was improved by Date fruit extract. Date stands as a useful food component and aqueous extract of date fruit causes inhibition of superoxide and hydroxyl radicals.<sup>24</sup>

The present study highlights the awareness to change towards the use of natural food and declares the protective potentials of the aqueous extract of Ajwa fruit on oviduct damaged by nicotine in rats. Active and passive smokers of reproductive age should be made aware of the possible hazards in smoking and how smoking could disturb their reproductive ability.

## Conclusion

In smoking women nicotine present in cigarettes either change structure or purpose of epithelial cells in the fallopian tube, which can result in infertility, ectopic pregnancy or spontaneous abortion. Ajwa fruit extract

normalized the damaged fallopian tube and can be used as a beneficial remedy to treat reproductive disorders.

**Conflict of Interest**

*None*

**Funding Source**

*None*

## References

1. Aslam HM, Saleem S, German S, Qureshi WA. Harmful effects of shisha: literature review. *International archives of medicine*. 2014;7(1):16.
2. Centers for Disease Control and Prevention. Smoking prevalence among women of reproductive age— United States, 2006. *MMWR Morb Mortal Wkly Rep*. 2008; 57: 849–852
3. Curtin SC, Matthews TJ. Smoking prevalence and cessation before and during pregnancy: data from the birth certificate, 2014. *Nat'l Vital Stat Rep*. 2016; 65(1): 1–14.
4. Saraiya M, Berg C.J, Kendrick J.S, Strauss L.T, Atrash H.K and Ahn Y.W. Cigarette smoking as a risk factor for ectopic pregnancy. *Am J Obstet Gynecol*. 1998; 178: 493-498.
5. Benowitz NL. Neurobiology of Nicotine Addiction: Implications for Smoking Cessation Treatment, *amjmed*. 2008; Vol 121 (4A), S3–S10.
6. Iranloye B. O. and Bolarinwa A. F. Effect of nicotine administration on weight and histology of some vital visceral organs in female albino rats. *Niger. J. Physio Sci*. 2009;24 (1): 7 – 12.
7. Cooper AR and Moley KH. Maternal tobacco and its implantation effects on fertility: More reasons to stop smoking. *Semin Reprod Med*. 2008; 26: 204-212.
8. Saeed K, Tahir M and Lone KP. Effect of phoenix dactylifera (date palm) pit powder on nicotine induced spermatotoxicity in adult albino mice. *JPMa*. 2015, Volume 65, Issue 1
9. Magers T, Talbot P, DiCarlantonio G, Knoll M, Demers D, Tsai I, et al. Cigarette smoke inhalation affects the reproductive system of female hamsters. *Reprod Toxicol*. 1995;9(6):513-2
10. Ruckebusch Y. Relationship between the electrical activity of the oviduct and the uterus of the rabbit in vivo. *J Reprod Fertil*. 1975;45:73–82.
11. Neri A, Eckerling B: Influence of smoking and adrenaline (epinephrine) on the uterotubal insufflation test (Rubin test). *Fertil Steril* 1969, 20:818-828.

12. Muhammad ghasemi F, Khajeh J S, Haji zadeh H, Homafar, MA, Saadat N. Protective effect of exogenous melatonin on nicotine induced changes in mouse ovarian follicles. *J Reprod Infertil.*2012; 13(3):143-150.
13. Bahmanpour S, Talaei T, Vojdani Z, Panjehshahin MR, Poostpasand A, Zareei S, Ghaemini M. Therapeutic effect of Phoenix dactylifera pollen on sperm parameters and reproductive system of adult male rats. *Iran J Med Sci.*2006;31:8-12.
14. Ali A, Abdu S, Antioxidant protection against pathological mycotoxins alterations on proximal tubules in rat kidney. *Func Foods in Heals & Diseases.* 2011; 4: 118-134.
15. Raieni SS, Fallahian M, Salehian MT, Jafri B and Ajoria L. Histomorphologic Effects of Smoking on Fallopian Tubes in the Rats. *I J Pathol.* 2009;4 (2): 85 – 87.
16. Morsy SA El-salam and El-Kholy SMS. The effect of methotrexate on the fallopian tubes of adult albino rats: a histological and immunohistochemical study. *Egypt J Histol.* 2012; 35:833-839.
17. Eweka AO, Eweka A and Om'Iniabohs F A.E. Histological studies of the effects of monosodium glutamate of the fallopian tubes of adult female Wistar rats. *N Am J Med Sci.* 2010; 2(3): 146–149.
18. El-abd S and Ibrahim M. Effect of sodium fluoride on the oviductal mucosa of adult albino rats and the possible protective role of pomegranate peel extract: a histological and immunohistochemical study. *Egypt J of Histology.* 2016;39(2):191-202 •  
DOI: 10.1097/01.EHX.0000490003.71440.40
19. Ghaly MA, Khedr E S G and Aleem AA. A comparative study of nicotine effect on the Liver of albino rat. *Egypt J Hospit Medic.* 2003;10: 130 – 144
20. Backhle, Y.S.; Hartiala, J.; Toivonon, H. and Votilla, P. (1979): Effects of cigarette smoke on the metabolism of vasoactive hormones in the isolated rat lung. *Br. J. Pharmacol,* 65, 495-499.
21. Gorrod, J.W. and Jenner, P. (1975): The metabolism of tobacco alkaloids. In *Essays in Toxicology,* 6, 35-78, New York.
22. Elsadek B, El-Sayed ES, Mansour A, Elazab A. Abrogation of carbon tetrachloride-induced hepatotoxicity in Sprague-Dawley rats by Ajwa date fruit extract through ameliorating oxidative stress and apoptosis. *Pak J Pharm Sci.* 2017;30(6):2183-2191.PMID: 29175788.
23. Wahdan RA and Alazouny ZM. Effect of monosodium glutamate on the fallopian tubes of adult albino rats and the possible protective role of vitamin C: a histological and immunohistochemical study. *Egypt J Histol* 2015; 38(1):68–76.
24. Al-Farsi M, Alasalvar C, Morris A, Baron M and Shahidi F. Comparison of antioxidant activity, anthocyanins, carotenoids, and phenolics of three native fresh and sun-dried date (*Phoenix dactylifera L.*) varieties grown in Oman. *J Agric Food Chem.* 2005; 21;53(19):7592-9.

#### Authors Contribution

**FF:** Conceptualization of Project

**MS:** Data Collection

**SN:** Literature Search

**TM:** Statistical Analysis

**AZ:** Drafting, Revision

**AS:** Writing of Manuscript