IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
www.iosrphr.org Volume 4, Issue 6 (June 2014), PP. 58-61

Galactagogue action of Nigella sativa seeds

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ABSTRACT: *This experimental study was designed to determine the galactagogue action of Nigellasativaseeds.*
LactatingmicewereswitchedontoNigellasativacontainingdietfromthedayoflabourandfor15days. Nigellasativasignificantly (P<0.0l) increased serum prolact in level and the weight of the Litter compared with controlgroup. Breasttissues of lactatingmicekepton Nigellasativacontain ingdietshowedlargeracini, thickerepitheliaandhyperactivity.Nohaematological,histologicalandbiochemicalsideeffectswerecausedby Nigella sativa.

Key words: *Nigella sativa, galactagogue, milk letdown*

الخلاصه:
لقد صممت هذه الدراسةالتجريبية لتحديد التأثير المدرر للحليب لبذور الحبه السوداء . تم إعطاءإناث الفئرانألعليقهالحاوية على الحبة السوداء من اليوم الأوللولادة ولغاية اليوم الخامس عشر ، لوحظ أن بذور الحبة السوداء أدت الى زيادة ملموسةإحصائيا(P<0.0l) في مستوى هرمون البرولاكتين في المصل وزيادةملموسةإحصائيافي أوزانالأجنة مقارنه بمجموعة السيطرة . كما أظهر نسيج الغدد اللبنية للفئران المعالجةزيادة في حجم الأسناخ اللبنيةوزيادة في ثخن الظهارة السنخية وفرط إفراز الحليب في معظم الأسناخ . لم تسجل تغيرات نسيجية أو دموية أو كيمياوية لدى الفئران المعالجة.

I. INTRODUCTION

Nigella sativa Linn (Black Cumin) is widely cultivated throughout South Europe, Syria , Egypt, Saudi Arabia, Turkey, Iran, Pakistan and lndia [(1)]. A1- Jassir has reported in detail the chemical composition of Nigellasativa seeds, theanalysisshowed a composition of20.85% protein, 38.20%fat, 4.64% mosit'ure, 4.37% ash, 7.94% crude fiber and 31.94% total carbohydrates [(2)]. Sodium iron, zinc, calcium, magnesium, manganese and, copper were detected in Nigella sativa seeds at low levels, while lead, cadmium and arsenic were not present [(2,3).] Chemical analysis of Nigella sativa fats, revealed a composition of myristic, palmitic, stearic, oleic, linoleic and arachidonic acids [(2, 3)]. However 67 compoundswereidentified ,by capillalygaschromatography of Nigella sativa oils.They contained p-cymene 31.7% , a- pinene 9.3% ,thymoquinone 24.5% and many othercompounds[(1)]. Nigella sativa carbohydrates consisted mainly of sucurose 32.56%,fructose21.72% ,α-glucose 20.81% and β-glucose 11.68%[(3)] . Analysis ofNigella proteins showed thatthey consisted of 15 amino acidsincluding 9 essentialaminoacids[(l)]. Nigella sativa seeds exerted many pharmacological effects, theseinclude antibacterial[(3-5)].antifungal[(3),] bronchodilator [(6-7)],inhibititon ofhistamine release from mast cells[(3,8)], anticholinergic and smooth musclerelaxant effects[(9)],cardiac depressant , hypotensive effects[(10,11)],hypoglycemic effects[(12)], immunostimulant[(13,14)]and anticancereffects[(15)].This study was designed to determine the galactagogue action of Nigellasativa seed and itssafety.

Materials and Methods:

Sixty mature female albino mice, of approximately similar bodyweightand agewereused in thisstudy. Theregularity ofestruscycleofthefemaleswasdeterminedby vaginalsmearstained by methyleneblue. Thenthe femaleswere mated with healthy malesofthe same strain, during theproestrusperiodandfor24hrs.Thedayoffertilization,asdeterminedbythe presenceofthesperm inthevaginal smears, wasconsidered asday 1ofthepregnancy. After labour,12 femaleswereexcluded becausethey gavelessthan 3 fetuses.The rest48 femaleswere divided into 2 groupsof24 each.The litter size was reduced to 3 fetuses for each female. Fetuses wereweighedand thenthe mothers ineach groupwereswitchedon controldiet orNigella sativa diet.Thedietwasprepared according to Agrawala*et al* [(17).]

Controldiet (1kg.) Nigella sativa containing diet (1kg.)

Wholewheatflour 800gr.Wholewheatflour 700gr
Wholemilk powder 170gr.Wholemilkpowder 170gr.
Yeast 22gr.Nigellasativapowder 100gr.
Calcium carbonate 5gr.Yeast 22gr.
Table salt 3gr.Calcium carbonate 5gr.
Multivitamins (SDI) 1capsule. Table salt 3gr.
Multivitamins(SD1)1capsule

Aslitterliveon mother'smilk only for20 daysand cannotnibbleat the food laid outforthem mothers [17], the experimentlasted for 15 days. Atday 15,fetuses were weighed again.Blood sampleswere taken from onethirdofthemothersineachgrouptodetermineserum prolactinlevel(R1A-ClSbiointernational-France).Blood samplesofthesecondthird ofthemothers in each groups were used to estimate serum glucose, urea,GOT,GPT,bilirubin,uricacid,creatinine,triglycerides,alkalineand acidphosphatasesbyanenzymaticmethods(Raudox).Bloodsamplesofthelastthird of the mothers were used to estimate WBC count, RBC count,differentialWBC countandHb .The breasttissues ofthe motherswere biopsied and processed forhistological examination. Specimens were taken from the liver, kidney,intestineandstomach forthepathologicalstudy.Studentt-testwasusedtodeterminethesignificancybetweengroups.

Results:

This study showed that serum prolactin level, oflactating femalemice kept on Nigella sativa containing diet, was significantly higher($P<0.01$)than thatofmothersswitchedontocontroldiet(Table1).Theweight of the litter ofthefemaleskeptonNigella sativa containingdietwas significantly ($P<0.01$)higherthanthoseoffemale givencontroldiet(Table 2).In comparison with control group,thesectionsofthebreast tissue of mothers kept on Nigella sativa containing dietshowed largeaciniwith an increaseintheproliferation andthicknessoftheepithelium.The majority ofthe aciniin the breasttissue showed moresecretaryactivity(Fig1).No pathological changes were observed in the liver,kidney,stomach andintestineoffemalesgivenNegillasativacontainingdiet.Allhematological and biochemicalvalues were not significantly changes.However,a slightreduction($P<0.05$)intheserum glucoseanduricacid wasfound in females keptonNigellasativa containingdiet.

Table 1: Serum prolactin level in females given control diet in comparison of female kept on Nigella sativa containing diet.

Groups	No. of mice	Serum prolactin ng/ml 8 p.m
Lactating mice on control diet	8	175.50 ∓ 7.82
Lactating mice on Nigella sativa containing diet	8	185.0 ∓ 3.16 ($p<0.01$)

Table 2 : The increase in the weight of the litter of the female mice kept on Nigella sativa containing diet compared with control.

Groups	The difference between the weight of the litter at 1st and 15th day of age (mg)*
The litter w eight of lactating mice on control diet	4730.25 ∓ 290.85
The litter weight of lactating mice on Nigella sativa containing diet	6168.66 ∓ 341.49 ($P<0.01$)

*Mean of the means of litter weight of all mothers in the group

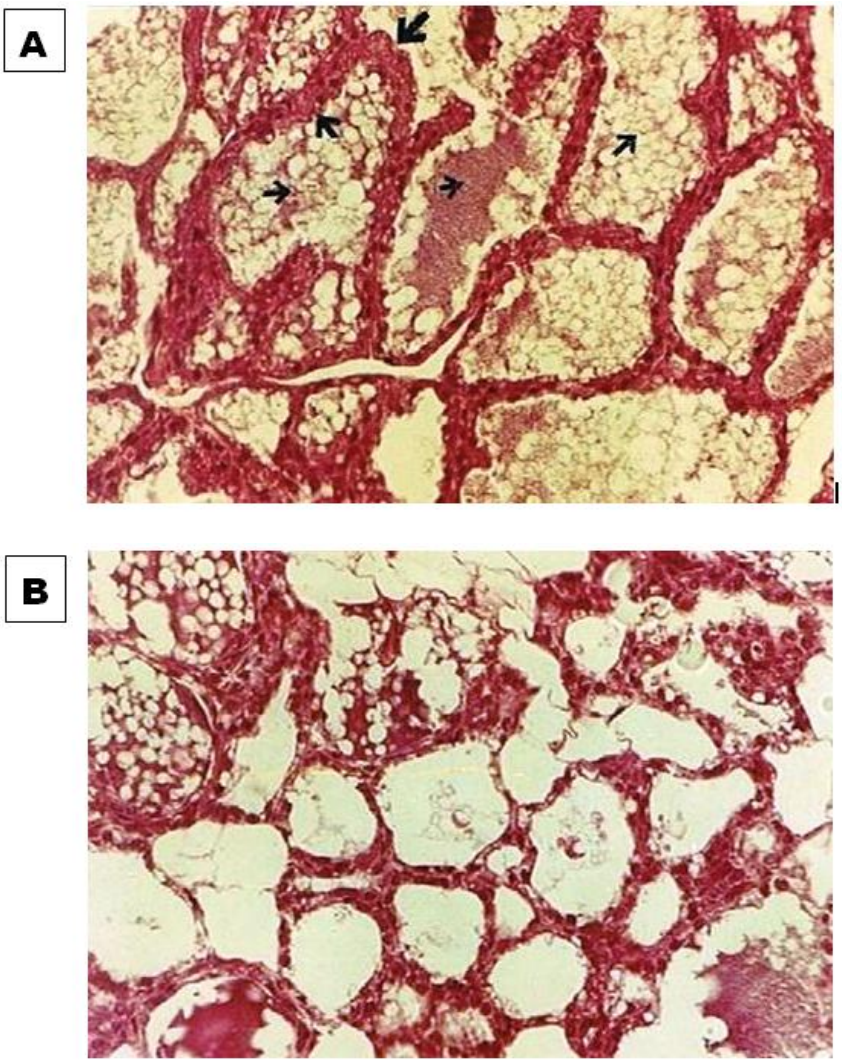

Fig.1: (A) Section on the breast tissue of the lactating mice kept on Nigella sativa containing diet showing larger acini (→),thicker epithelia (→), and more secretory activity(→), compared to the breast tissue of the lactating mice kept on control diet (B). (40X).

Discussion:

The prolactin stimulatory effect of Nigella sativa could be attributed to its anticholinergic effect [9] .Snyder *et al* found thatlactotrophs contained muscarinic receptors,and the administration ofcholinergic muscarinicagonistdecreased the prolactin secretion eitherin basalcondition orafterdifferentstimuli[18],in addition tothisdirectmuscarinic effect at the level of lactotrophs, acetylcholine also seems to inhibit prolactin release at the level of hypothalamus [19]. On theotherhand,nigellone,the carbonyl polymer ofthymoquinoneisolated from Nigellasativa,is a very effective histamine releaseinhibitor.Thisinhibition ismediated by decreasing intracellularcalcium,inhibition ofprotein kinase C and inhibition of oxidative metabolism [8]. Histamineisan inhibitory mediator on the secretion ofprolactin atthelevelofhypothalamus.Thisinhibition is mediated by H2 receptors [20]. Therefore the prolactin
stimulatory effect of Nigella sativa could be attributed to itsanticholinergic and antihistaminic actions.Furthermore, Nigella sativacontained high amounts of carbohydrate, oils, proteins and trace elements [2, 3]. These contents represent a high energy sourceswhichcould participate in the galactagogue effect of Nigella sativa.Thehyperactivity of the breast tissue of the lactating miceonNigellasativa containing diet, occur due to an increase in the prolactinsecretion. Theseeffectswereclearly reflected on thelitterweight.According to these results, it appears that Nigella sativa is free from histological, haematological and biochemical side effects.Thesafety of Nigella sativa was recorded by manypreviousstudies[1, 12, 14].However, thedeclinein theserum glucoseanduricacidwasattributedto hypoglycemic [12], and hypouricemic effects of Nigella sativa [1].

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