



**To the soul of the dearest person  
on this planet: my mother.**

**and**

**To my father, family and friends.**

***Awatif***

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## **Abstract**

Three experiments were carried out in this research work during 2008 – 2009 in order to investigate the potentiality of two medicinal plants, *Cardiospermum halicacabum* L. and *Croton tiglium* seeds, possessing toxic properties on albino rats, and to investigate for properties of *Croton tiglium* seed as an anti – fertility and anti – implantation on female albino rats.

Preliminary phytochemical screening showed that both plants contained flavonoids and saponins but Croton seeds contain high alkaloids content while *Cardiospermum halicacabum* contains tannins and appreciable amount of cynoglycosides. No anthraquinone glycosides were detected in both plants.

Albino rats of about 6 – 8 weeks age and of an average body weight between 120 – 180 grams and of both sexes were used for this study.

After the acclimatization period, the animals were subjected to 3 experiments as follow:

1. Experiment I: Toxicity of *Cardiospermum halicacabum* on Albino Rats:

Eighteen male albino rats of age 6 – 8 months and 120 – 160 gms body weight were randomly divided into 3 groups. Group 1 served as control which given normal diet (300gms meat+ 700gms wheat, water corn oil and salt/ killo) purchased and given to the rats by the technicians of NCR,, while group 2 and group 3 were given daily diet contained 10% and 30% *C. halicacabum* powder respectively. Feeding continued daily for 4 weeks.

No clinical signs were observed in the treated groups, and they look normal, without behavioral changes observed. No mortality recorded. A progressive body weight gain of the animals was observed in the three groups.

The serum biochemical parameters showed no statistical differences in glucose concentration between control animals ( group 1) and animals in group 3, total protein and globulins also exhibited the same manner, no statistical changes from control value were seen, but remarkable significant reduction from control value was seen in albumin and urea levels at ( $P \leq 0.05$  ). Lipids profile (total cholesterol and triglycerides), showed slight reduction in cholesterol value from control, but of no statistical significance, in both treated groups of animals, but triglyceride showed remarkable significant decrease compared with control value. The result also showed that enzyme activities of AST (Aspartate Transferase) and ALP (alkaline phosphatase) showed no remarkable significant changes from control values in both groups of animals under treatment (group 2 and group 3), but the activity of the enzyme ALT (Alanine Transferase), showed remarkable rise activity.

The haematological results showed no remarkable changes over control value. Histopathological examination of some animal's body organs showed some changes occurred in small intestine and liver but of no clinical significance. The mentioned changes were of minor alterations, but of no clinical significance.

These results and findings may suggest that *Cardiospermum halicacabum* given as powder at concentrations of 10 % and 30 % mixed with the diet of the experimental albino rats for 28 days may had mild toxic effect on the animals these reflected in histopathological investigations on the intestine, liver and heart in which some histopathological alterations occurred and this also may not exclude the presence of toxic or lethal compounds in the plant.

## 2. Experiment II: Toxicity of Croton Seeds on Albino Rats:

The second experiment which aimed to test the toxicity of *Croton tiglium* seeds on the experimental animals grouped in three groups treated as control group (group I) given normal animal diet, group II and group III given a 10 % and 20 % respectively of the Croton seeds mixed with animal diet for 2 weeks.

The result revealed that animals in group I maintained normal body weight and looks normal throughout the 2 weeks of the experimental period, while animals in groups II and group III showed decrease in the body weight. Decrease in appetite, clinical signs such as watery diarrhea appeared few hours after the ingestion of the diet, no death occurred among the animals of treated groups who fed a diet containing 10% and 20 % of *Croton tiglium* seeds. The results also indicated that Croton seeds treatments brought about remarkable change on biochemical, haematological and histopathological parameters.

### 3. Experiment III: Anti - fertility and Anti - implantation Effect of Ethanol and Petroleum Ether Extract of *Croton tiglium* Seeds on Female Albino Rats:

Croton seeds extracts were also tested. Petroleum ether Croton seeds extract administrated at a concentration of 200 mg/kg body weight daily for 7 days exhibited minor biochemical, haematological, and histopathological effects on the tested animals, but ethanol Croton seeds extract administrated at the same concentration resulted in profound alteration as mentioned in the treatment of animals with 20 % Croton seeds.

As far as the antifertility and anti – implantation properties of the ethanol and petroleum ether extracts of the Croton seeds on the female animals, are concerned, the treated female animals were mated for 14 days with males after it subjected to treatment of petroleum ether seeds extract or

ethanol seed extract, during which the animals were observed and signs of pregnancy were observed followed by examination of sexual and reproductive organs of the animals.

The results revealed that female animals under petroleum ether extract treatment exhibited remarkable delay of pregnancy up to 3 months compared with control females who performed normal carriage and pregnancy and delivered at term, but the delivered litters although less in number compared with control females, and no complete absence of implantation in animal uterine horn occurred. But female rats of group II who treated with 200 mg/kg body weight daily for a week ethanol Croton seeds extract has showed 100% effective in preventing implantation sites in uterine horn of females animals.

It has been postulated that endometrium of the animals uterus may be histopathologically affected resulted in decrease of contact and adhesion between blastocytes and uterine epithelium since histopathological examination of uterus indicated atrophy glands, odema and erosion of uterus superficial layers.

### **ملخص الدراسة**

تم اجراء ثلاث تجارب بحثية فى الفترة من 2008 - 2009م وذلك

بغرض البحث فى

سمية اثنين من النباتات الطبية *Croton* و *Cardiospermum halicacabum* و *tiglium* وايضا دراسة امكانية بذور نبات *Croton tiglium* كمواد مانعة للحمل ومانعة لتعشيش البويضة عند اناث حيوانات التجارب والتي هى الفئران البالغة . Albino rats .

اما حيوانات التجارب فقد تم شراؤها من وحدة ابحاث النباتات الطبية والعطرية بالمركز القومى للبحوث بالخرطوم عند اعمار تتراوح بين 6 - 8 اسابيع وبمتوسط اوزان تتراوح ما بين 120 - 180 جرام ومن كل الجنسين.

عمل مسح كيميائى phytochemical screening لمعرفة المكونات الفعالة او السامة للنباتات الطبية المستخدمة فأوضح نتيجة المسح الكيميائى الاولى لهذه النباتات ان كلا النباتين تحتويان على مواد فعالة مثل الفلافونيات والصابونيات، مع وجود نسبة عالية من القلويدات فى بذور نبات ال *Croton tiglium* فى حين ان نبات ال *Cardiospermum halicacabum* يحتوى على نسبة عالية من التانينات وكمية بسيطة من الجلايكوسينات ، ولكن لم يظهر المسح الكيميائى وجود جليكوسيدات الاتنوسيانين فى اى من النباتين. ثم اجريت التجارب بعد فترة اقل من اسبوع على النحو التالى:

### **1. التجربة الاولى :**

استخدمت فى هذه التجربة 18 فارا من الذكور وذلك بغرض دراسة سمية نبات ال *Cardiospermum halicacabum* على حيوانات التجارب. وقسمت الحيوانات الى ثلاث مجموعات بمعدل 6 فئران فى كل مجموعة ، حيث وضعت فئران التجربة الاولى والتي هى المجموعة الضابطة ( Control ) وضعت تحت غذاء الحيوانات العادى طوال فترة التجربة والتي امتدت لفترة 4 اسابيع. اما المجموعة الثانية فتغذت غذاء يحتوى على خليط من مسحوق نبات ال *Cardiospermum halicacabum* بنسبة 10% اما المجموعة الثالثة فكانت تحت غذاء به نسبة 30 % من مسحوق نبات ال *Cardiospermum halicacabum* وتمت مراقبة الحيوانات من المجموعات



الثلاث طوال فترة التجربة وتسجيل سلوك هذه الحيوانات والحالة الصحية لها وتسجيل اى حالات اعياء او تسمم مع مراقبة أوزانها.

بعد انتهاء التجربة وعمل القياسات وتحليل العينات من الدم والانسجة لبعض الاعضاء الداخلية لهذه الحيوانات كانت النتائج كالتى:  
فقد اوضحت النتائج ان كل حيوانات التجارب فى المجموعات الثلاث وطوال فترة التجربة كانت ذات حالة صحية جيدة ولم تظهر عليها اى اعراض الفتور او اعراض السمية مع ملاحظة الزيادة المطردة فى اوزانها مقارنة باوزانها قبل اجراء التجربة.

عند اجراء التحليلات المعملية للمكونات الحيوية ومكونات الدم، وبعض اعضاء تلك الحيوانات اتضح ان هناك بعض التغيرات ولكن ليست ذات دلالة مرضية عند مقارنتها بالمجموعة الضابطة فمثلا ليست هناك تغيرات ذات دلالة احصائية معنوية فى تركيز سكر الدم بين المجموعة الضابطة والمجموعة تحت المعاملة 30% وايضا لا يوجد تغير يذكر فى تركيز كل من البروتين الكلى والقلوبولينات، لكن كانت هناك تغيرات ذات دلالة معنوية فى تركيز اليوريا والاليومين.

اما نتائج فحص الدهون فكان هناك انخفاض بسيط وليس ذو دلالة معنوية فى تركيز الكوليستيرول الكلى مقارنة بالتركيز فى المجموعة الضابطة ( كترول) فى كلتا المعاملتين ، لكن اظهرت الجلسيريدات الثلاثة انخفاض ملحوظ وذو دلالة احصائية معنوية مقارنة بالمجموعة الضابطة. كما اوضحت الدراسة ايضا أن معاملة الفيران بتراكيز 10% و 30% من نبات ال *Cardiospermum halicacabum* ليست لها تأثير يذكر على مستوى نشاط كل من انزيمى AST و ALP فى كل من المجموعتين تحت الاختبار مقارنة بالكنترول ، اما الانزيم ALT فقد اظهر زيادة معنوية عن القيمة الضابطة. اما فحوصات مكونات الدم Hematological studies Hb, PCV, RBC, MCV (and MCHC ) لم تظهر اى تغيرات ذات دلالة احصائية معنوية فى كل من الحيوانات فى كلتا المجموعتين مقارنة بالمجموعة الضابطة اما دراسات

فحص الانسجة المريضة لبعض عينات من الاعضاء الداخلية لتلك الحيوانات فظهرت تغيرات نسيجية ليست ذات دلالات مرضية كما فى حالة الامعاء الدقيقة والكبد. وتخلص تلك النتائج الى ان نبات *Cardiospermum halicacabum* عند اضافتها بتركيز 10% و 30% لفيران التجارب لمدة 28 يوم ربما يكون ذات سمية معتدلة وليست حادة وظهر ذلك فى بعض التغيرات النسيجية فى كل من الكبد والامعاء الدقيقة والقلب بالرغم من ان الفئران كانت فى حالة صحية ولم تظهر عليها حالات تسمم بصورة واضحة كما انه لا يستبعد وجود بعض المركبات السامة فى هذا النبات ادت الى حدوث هذه التغيرات السمية المعتدلة.

#### \*التجربة الثانية :

وتهدف هذه التجربة ايضا الى دراسة سمية بذور نبات ال *Croton tiglium* على فئران التجارب عند اضافتها لغذاء الحيوانات بتركيز 10% و 20% لمدة التجربة التى كانت اسبوعان اوضحت نتائج التجربة ان فئران المجموعة الاولى والتى وضعت تحت غذاء خالى من اى اضافات نباتية (معدة من قبل تقنى المركز القومى للبحوث من خليط من 300 ملجم من الدقيق مع 700 ملجم من الدقيق والماء وملح وقليل من الزيت للكيلو الواحد) ولنفس المدة كانت ذات نمو طبيعى عادى وزيادة مضطردة فى اوزانها اما حيوانات المجموعة الثانية والتى وضعت تحت غذاء خليط من بذور ال *Croton tiglium* بتركيز 10% وايضا المجموعة الثالثة والتى تغذت على غذاء خليط بنسبة 20% فكان هناك انخفاض ملحوظ فى اوزان تلك الحيوانات عند انتهاء التجربة مقارنة باوزانها عند بداية التجربة، وان كمية الغذاء التى تناولتها الحيوانات تتناسب مع اوزانها المنخفضة. علاوة على ظهور حالات اعياء واسهالات مباشرة بعد ساعات من بداية المعاملات فى كلتا المجموعتين ولم يصاحب بموت الحيوانات ولكن اعراض السمية كانت اكثر وضوحا فى المجموعة

الثالثة تحت الغذاء المحتوى على تركيز 20% من بذور ال *Croton tiglium* مما يستنتج ان بذور نبات ال *Croton tiglium* تحتوى على مواد او مركبات لها تأثير سام على حيوانات التجارب عند التراكيز المذكورة اعلاه وان التأثير الاكثر فعالية عند تركيز 20% من بذور نبات ال *Croton tiglium* ويعتقد ان ظهور حالات التسمم والتي تزداد حدتها فى بعض حيوانات التجربة عند المعاملة بالتراكيز المذكورة اعلاه من بذور النبات تحت الدراسة ربما ترجع الى وجود بعض المركبات السامة التى توجد فى بذور نبات ال *Croton tiglium* .

### \*التجربة الثالثة :

لدراسة تأثير المستخلص الكحولى (ايتانول ) لبذور نبات ال *Croton tiglium* وايضا مستخلص ايثر البترول وايضا لدراسة امتلاك بذور نبات ال *Croton tiglium* خاصية اعاقه او منع الحمل عند اناث الفئران وايضا اعاقه او منع تعشيش البويضات فى جدران الرحم . فقد عوملت اناث فيران التجارب لمستخلص ايثر البترول وايضا مستخلص كحول الايثانول لبذور نبات *Croton tiglium* لمدة اسبوع، ثم جمع الأناث مع الذكور لمدة اسبوعين للتزاوج. اتضح ان معاملة مستخلص الايثر البترولى بتركيز 200 ملجم/ كجم يوميا ولمدة اسبوع لها تأثير ضعيف على بعض المكونات الكيماوية ومكونات الدم فى بعض حيوانات التجارب فى حين ان المستخلص كحول الايثانول كان اكثر فعالية فى حدوث تغيرات ذات دلالة مرضية. وان مستخلص الايثر البترولى له تأثير ضعيف على خصوبة الحيوانات مثل تأخير فترة الحمل لمدة 3 اشهر وايضا على عدد الانجاب ولكن لا توجد حالة عقم ولا يوجد حالة اعاقه تعشيش البويضة فى جدار الرحم واضحة . اما مستخلص كحول الايثانول للبذور فذو تأثير قوى وواضح فى منع الحمل عند الاناث وايضا منع تعشيش البويضة فى جدران الرحم منعا كاملا ولا توجد حالات حمل او انجاب بين الحيوانات ونخلص هذه النتائج الى ان المستخلص الكحولى ( ايتانول) لبذور نبات ال *Croton tiglium* اكثر فعالية فى اعاقه الحمل وتعشيش البويضة فى

جدران الرحم بدرجة 100% من الاعاقة. ونخلص هذه التجربة الى ان بذور نبات ال *Croton tiglium* ذات خواص مانعة للحمل والانجاب وتعشيش البويضة فى جدران اناث حيوانات التجارب.

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