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Ricinus communis-linn (castor plant), male contraceptives and reproductive health of women

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Abstract

The medicinal use of castor plant is extensive. Castor oil is most commonly used as a laxative, and the leaves and seeds have been used to augment labour, promote lactation and to treat syphilis and leprosy. Its use for contraception is an ancient practice among the *Rukuba* women of Plateau State in Nigeria, who would chew 2-3 seeds for contraceptive coverage of one year. The acute and chronic spermatogenic effect of the minor seed variety of *ricinus communis-linn* is hereby reported. Thirty male rats weighing 200–250g were grouped (n = 5) and treated with the *n*-hexane extract of the seeds, each made up to 1ml with physiological saline, and given as a single dose, intraperitoneally. Control groups had 1 ml physiological saline. Semen was collected 72 h and 6 weeks after treatment and analyzed within one hour of collection. The seed extract suppressed spermatogenesis and sperm motility up to six weeks after treatment. But semen parameters reverted to normal values in the 7 weeks of treatment, showing primary spermatocytes and spermatids in the seminiferous tubules. Our results showed *ricinus communis-linn* to be a potent but reversible anti-spermatogenic agent with significant anti-motility properties. Moreover, being of plant origin, it is readily available and affordable. We hereby present *ricinus communis-linn* as a possible male contraceptive agent that can relieve women of their reproductive burden globally. *(Afr J Reprod Health 2021; 25[4]: 135-141).*

Keywords: *Ricinus Communis-Linn*, male contraception, reproductive health, women

Résumé

L'utilisation médicinale de la plante de ricin est étendue. L'huile de ricin est le plus souvent utilisée comme laxatif, et les feuilles et les graines ont été utilisées pour augmenter le travail, favoriser la lactation et traiter la syphilis et la lèpre. Son utilisation pour la contraception est une pratique ancienne chez les femmes Rukuba de l'État du Plateau au Nigeria, qui mâchaient 2-3 graines pour une couverture contraceptive d'un an. L'effet spermatogène aigu et chronique de la variété mineure de graines de ricinus communis-linn est rapporté ici. Trente rats mâles pesant 200 à 250 g ont été regroupés (n = 5) et traités avec l'extrait de n-hexane des graines, chacun complété à 1 ml de sérum physiologique et administré en une seule dose, par voie intrapéritonéale. Les groupes témoins avaient 1 ml de sérum physiologique. Le sperme a été collecté 72 h et 6 semaines après le traitement et analysé dans l'heure suivant le prélèvement. L'extrait de graines a supprimé la spermatogenèse et la motilité des spermatozoïdes jusqu'à six semaines après le traitement. Mais les paramètres du sperme sont revenus à des valeurs normales au cours des 7 semaines de traitement, montrant des spermatocytes et des spermatides primaires dans les tubules séminifères. Nos résultats ont montré que le ricinus communis-linn est un agent anti-spermatogène puissant mais réversible avec des propriétés anti-motilité significatives. De plus, étant d'origine végétale, il est facilement disponible et abordable. Nous présentons ici le ricinus communis-linn comme un agent contraceptif masculin possible qui peut soulager les femmes de leur fardeau reproductif à l'échelle mondiale. *(Afr J Reprod Health 2021; 25[4]: 135-141).*

Mots-clés: Ricinus Communis-Linn, contraception masculine, sante reproductive, femmes

Introduction

Family planning has been proven to improve maternal and child health, but the accompanying side effects present a major clinical problem[1-2]. While there are many successful female contraceptives, vasectomy and condoms are the most effective in males[3]. It has been said that all of the contraceptive methods known, present with one or more problems[1]. Methods currently used by females include injectables, intra uterine devices (IUDs), vaginal rings, patches, implants, condoms, oral pills, sterilization on the one hand, and lactational amenorrhea techniques, coitus interruptus, and awareness-based methods on the other hand[4]. WHO records of 2011 however, show

that 210 million pregnancies occur annually all over the world. Out of this, 80 million are unplanned, thus promoting unsafe abortion[5] and avoidance of conventional contraceptives[5]. These range from weight gain and menstrual bleeding to cardiovascular complications and cancers[6] and are found to be minimal with a reduction in the hormonal dosage[2]. Irregular bleeding is the commonest reason for the discontinuation of problematic contraceptive methods[4]. Over the years, it has become certain that the use of current birth control methods presents with health complications that are severe enough to warrant clinical care and management of these side effects[7]. Because conventional female contraceptive agents often have severe health repercussions and since male anti-fertility agents are uncommon, some couples may be left with no contraceptive options. This calls for the need to find alternative methods that are less problematic to women of reproductive age. Even better still, a non-hormonal male contraceptive drug since most male contraceptives used in clinical trials consist of testosterone combined with other hormones. Unfortunately, the effect of long-term use is yet to be ascertained[8]. Furthermore, efforts are being made to find male contraceptive agents that have potent anti-spermatogenic effects but do not interfere with Leydig cell function. Spermatogenesis is a continuous process that begins at puberty and is regulated by pituitary testicular and adrenal hormones. Spermatocytes take approximately 72 days to mature. They travel through the seminiferous tubules to the epididymis, where they are stored prior to ejaculation[2].

Castor plant

Castor plant also called castor oil plant and castor beans belongs to the family of Euphobiaceae and is popular for its yield of castor oil. It is commonly a shrub of 8-12 feet but can be 20-30 feet (e"10m) high[9] (USDA, 2016). Each tree bears both male and female flowers, which occur in clusters, upper (male) and lower (female) flowers.

The seed has three lobes, each lobe containing a seed, which is smooth and elliptical in shape[10]. They exhibit extreme variation in size and colour; they may be grey, brown, black, or brown/black mottled with a size of 0.8-1.8cm in length, 0.4-1.2 cm in width, and oval or compressed in shape[11]. They are 17 varieties of the seeds[11] which are classified into 3 varieties; variety major (or the large seed variety) variety intermedia (or medium seed variety) and various minor or small seed variety).

Many advances have been made in the molecular biology of castor seeds. Its seedlings contained more than 100 different polypeptides against which a complex of antiserum has been raised[12]. Furthermore, the castor plant expressed auxin-related gene family, that regulates hormone signaling pathways in plants. These genes, therefore, regulate growth and stress response and have been associated with functional diversification in plants[13]. The seed contains about 20% shell and 80% kernel. Both consist of about 58-66% oil[14]. Trease and Evans recorded a fixed oil yield from the castor seed, of 55-60%. Other constituents include 20% proteins; ricin (toxalbulmin) albumin; enzymes (e.g. lipase, chymase); nucleoalbumin; amino acids; globulins, glycoproteins, and alkaloids, steroids, and elements (magnesium, calcium, and manganese. Its toxicity is attributed to the protein content, ricin, constituting 5%[15,11].

Clinical trials with Ricinus Communis-linn

The use of castor seeds for contraception is widespread among the Rukuba tribal women of Bassa local government area in Plateau State, Nigeria[16-18]. In 1990, this property of castor seeds was thrown into the limelight when a female traditional doctor (called Hazija), communicated that 2-3 seeds protect the female from conception for a whole year[19-20]. This information has led to an enormous amount of research work on the seed between 1990 until date. Prior to this, most work done on castor seed has been from the aspect of toxicity. More interestingly, some other researchers have reported on the antifertility property of the seed[21-22]. Furthermore, 10 women volunteers, oral administration of 3 seeds prevented contraception for 12 months with no sign of toxicity[19].

Many plants and herbs have contraceptive properties[19,23-24]. *Ricinus Communis-linn* showed an anti-ovulatory effect in Wistar rats[25] and in a reversible manner [25-30]. However, there is a dearth of data on its mechanism of action and antifertility

properties in male animal subjects. Moreover, this has not been investigated in men. Thus, the aim of this work is to investigate the anti spermatogenic properties of the N-Hexane extract of *ricinus communis-linn* in adult male Wistar rats.

Methods

Seed extraction

The seeds were extracted after the method of Okwuasaba *et al*[31]: Dried seeds (100 g) were ground into a fine powder using a mortar and pestle and soxhlet extracted for 72 h in 350 ml of *n*-hexane at 30°C. The extract was then concentrated in a water bath at 59.0 ± 1°C, dissolved in an appropriate volume of corn oil, and stored at 4°C.

Animal treatment

With ethical clearance, thirty male Wistar rats were raised to weigh between 200 and 250g and acclimatized for two weeks prior to the experiment. They were divided into treatment groups (n = 5). 10 mg/kg extract was administered to each test rat intraperitoneally through the anterior abdominal wall. Out of 10 test rats, 5 were euthanized after 72 h to observe the acute effect of the seed extract on semen parameters, and the other set (5), after 6 weeks in order to observe the chronic effect of the extract on semen quality. 10 control rats had equal volumes of physiological saline, 5 rats were sacrificed after 72 h and the other 5 after 6 weeks. All subjects were weighed weekly, fed with Pfizer pellets, and had water *ad libitum.* They were sacrificed in the 7th week of treatment using a chloroform chamber. The testes were exposed by an incision on the ventral surface of the scrotum, through which the caudal epididymis was excised, fenestrated, and placed in 1 ml of saline for semen analysis. A scientist that was blind to the experiment analyzed all semen samples within one hour of collection.

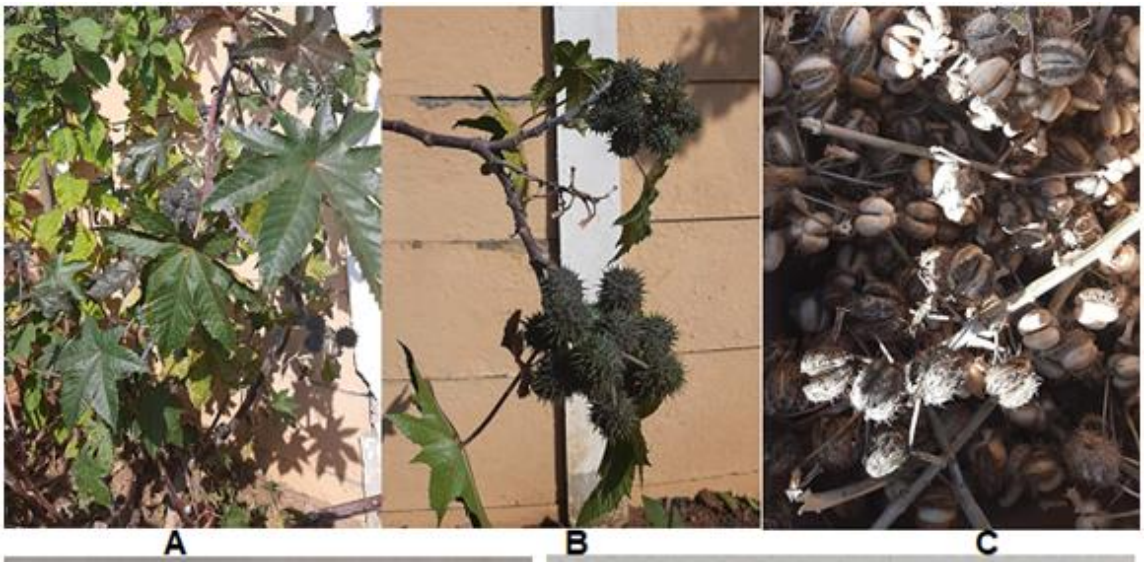
Results

As determined by microscopic analyses, the appearance, liquefaction, and consistency of all semen samples were normal. The extract suppressed semen parameters (mean count, motility, and morphology) within 72 hours of treatment; there was a 50% reduction in the percentage mean normal forms (40%) when compared to the control subjects (80%). While the percentage mean motility was reduced to 56% in test rats, (control value was 88.0%). The percentage mean count was the most affected (49 ($x10^6$). It was 99.5 ($x10^6$) in the control group. Mean normal forms and motility improved over the next few weeks to 60 and 65 respectively but the mean count was 39 (x10 6) in the 6th week, returning to values comparable with those of control rats only in the 8th week of treatment. Unlike Mean normal forms and Mean motility that showed significant improvement within six weeks, semen counts began to recover only at that time. This is attributed to the fact that the formation and maturation of spermatocytes take about 72 days[32].

Discussion

In our previous work, we found castor seed to be a potent anti-ovulatory agent with oestrogen-like properties. In addition, cervical screening of women who had been on castor seeds for over five years yielded no side effects, as is common with conventional hormonal medicines. Female contraceptives are diverse, but male contraceptives tend to target semen parameters and are therefore specific in their function - to prevent pregnancy[8]. The seed of *ricinus communis-linn* is widely used around the world for traditional medicinal practices[9]. The seed extract suppressed the ovarian cycle of adult cyclic Sprague-Dawley rats[6] and suppressed testicular function in a way similar to the anti-androgenic drug, cyproterone acetate[7]. Semen parameters determine male fertility[10]. Routine semen analyses assess multiple parameters including appearance, volume, liquefaction, concentration or viscosity, agglutination, hydrogen ion concentration, leucocyte count, sperm count, motility, viability and vitality, the morphology of spermatocytes, and anti-sperm antibodies[11].

Semen samples from the treatment groups showed azoospermia, with the percentage of normal morphologies being 40% (acute effect experiment), compared to 80% for the solvent control subjects. These values both improved to 60% and 86% respectively after six weeks of treatment.



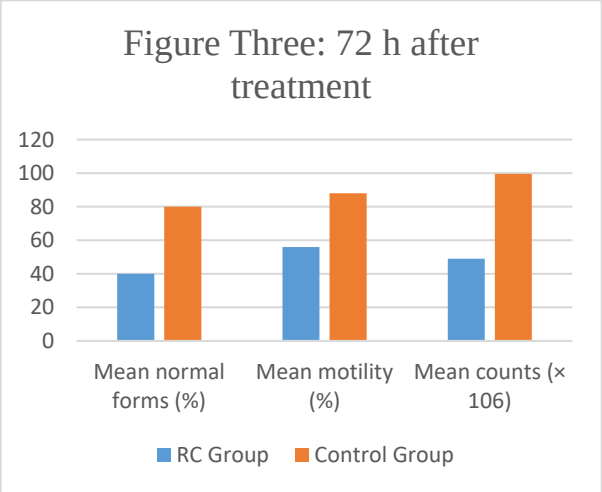
A), fresh clusters of castor seed, B) and dried castor seeds, C)

Figure 1: The minor seed variety castor plant

shows the sizes of the seeds in centimeters; each seed is about 1.1cm long. The seeds were obtained from the Department of Pharmacology, University of Jos, Jos, Plateau State, Nigeria

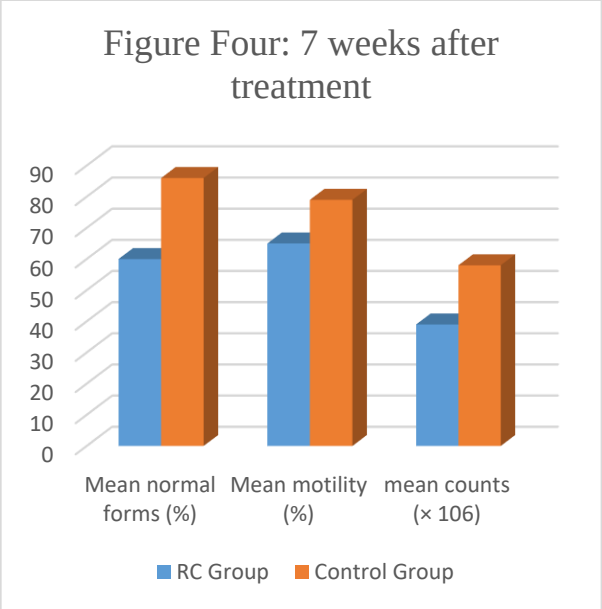
Figure 2: The minor seed variety of castor plant (D) used in this study. Image E)

Why improvement in the control semen parameters? This may be because of relief from the stress of being experimented upon. The sympathetic nervous system and the adrenal cortisol regulate acute and chronic stress respectively. Unfortunately, these responses to stress, affect negatively, the reproductive system[12]. Moreover, 5% of cases of infertility are due to emotional factors with neuroendocrinology and reproductive disruption[13]. Stress has been linked to poor semen quality; stress inhibits both the central control of reproduction and local testicular response (the hypothalamic–pituitary–gonadal axis). This reduces testicular androgen production[14]. Reducing stress in the subjects may therefore alter semen values. Therefore, in this work, we created a control group that received no treatment or interruption whatsoever, and so, these were the least stressed. Mean sperm counts for test subjects was 49×10^6 in 72 hours compared to 99.5×10^6 in control rats. The mean percentage of sluggish and non-motile cells was 44% with acute treatment that further decreased to 35% in six weeks. However, there was evidence of improving testicular functions (the presence of immature spermatocytes and spermatids). There was improved sperm motility



Note the marked acute suppression of sperm cell count and motility

Figure 3: Sperm morphology, count, and motility after 72hrs. Note the marked acute suppression of sperm cell count and motility



There is suppression of cell count and cell motility but note that semen parameters are returning to normal (seen here as improving values).

Figure 4: Sperm morphology, count, and motility after 7 weeks

from 56% acutely to 65.3% in the test rats after 6 weeks (65.3%) in comparison with 88% and 79% in the respective control rats. A decrease from 88% to 79% can be attributed to experimental stress. Sperm morphologies were not affected by treatment but an assessment of the functional capacity of the cells can be confirmed (e.g. by mating treated rats with proven females). This may be more revealing but is outside the scope of this work.

The anti-spermatogenic effects of drugs and toxins may be due to their interference with Leydig cell function or steroidogenesis. Critical cellular processes that control steroidogenesis include the delivery of cholesterol into the mitochondria and steroidogenic enzyme expression in Leydig cells[15]. Disruption of Leydig cell functions, therefore, leads to reduced androgen production. *Ricinus communis-linn* contains agglutinin that binds to galactose, lactose, and their derivatives[16]. This reduces semen fructose, the major source of energy for spermatocytes, and may be responsible for the reduced motility (sluggishness) observed in this work. Nevertheless, this study revealed castor seed to be a potential male contraceptive agent that targets the process of spermatogenesis and motility of spermatocytes in particular, both in a reversible manner.

Conclusion

It is the right of the individual to access a preferred anti-fertility method. However, a method based on the male factor is simpler when compared to the diverse methods currently used by women. Moreover, the use of male contraceptives will reduce the stigma associated with the female on family planning. This work presents the possibility of a cheap, readily available, and potent, but a reversible male contractive agent of plant origin. The use of castor plant may be more acceptable culturally and religiously. It will not only improve female reproductive health but also alleviate the high female morbidity and mortality rates associated with conventional contraceptives.

Limitations

In future work, the effect of the extract on the ultrastructure of seminiferous tubules will be examined. Also, Leydig cell count and function will be evaluated. Moreover, the scope of this work does not address the effect of the extract on sperm capacitation.

Conflict of interest

The Authors have no conflict of interest in this work.

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