

THE SEEDS OF CASTOR OIL PLANT (*RICINUS COMMUNIS* LINN.) AS A HERBAL ORAL CONTRACEPTIVE – A REVIEW

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SUMMARY.

Castor oil plant (*R. comunis* L.) has been used extensively in the different parts of the world as medicament for the treatment of different ailments. As oral herbal contraceptive, *R. communis* L. has been used in the middle belt of Nigeria, Saudi Arabia, Iraq and the Middle East in general. The seed's efficacy as a contraceptive drug has been confirmed by both Scientists in Nigeria and other Countries worldwide. The physical properties of the seeds has been documented by the African Pharmacopoeia and the toxicity of the seeds as a herbal contraceptive drug has been established to the greater that one gramme with a wide margin of safety.

Formulation studies have produced two dosage forms (tablets and capsules) whose quality was comparable to conventional tablets and capsules. The dosage forms have the potential to result in the production of a novel depot contraceptive herbal drug from our locally grown castor oil plant, which could revolutionize contraceptive therapy by its once, a year regimen.

INTRODUCTION.

The seeds of *R. communis* Linn. (Fam. Euphorbiaceae) have been extensively used by traditional healers as oral

contraceptive in Africa. Three small seeds are usually decoated and swallowed on the third days of the menstrual period(1). It has been reported by researchers in Saudi Arabia and Iraq that the seeds of *R. communis* Linn are also taken for contraceptive purposes. Three intact seeds are used on the first day of menstruation as oral contraceptive in Saudi Arabia(2). In Iraq, traditional healers also use the seeds as an infertility drug(3). In the middle belt of Nigeria, three seeds of *R. communis* Linn. are administered once by traditional healers to women as contraceptive drug for a duration of one year(1). Okwuasaba et al 1991 and Isieche et al, 1997, have shown that these seeds have significant contraceptive efficacy with minimal side effects(4,5).

MORPHOLOGY AND PHYTOCHEMISTRY.

The castor oil plant, (*R. communis* Linn.) that is indigenous to India and comprising about 17 varieties, is now diffused all over tropical and sub-tropical countries. In India it may attain a height of 40m and be a perennial tree, but in temperate savannah climate it is either a shrub or an annual herb(6). The large arborescent forms yield large seeds, while the small annual varieties yield small seeds(6,7).

The seeds have been broadly classified into three groups depending on size: large size (variety major), medium size (variety intermediate) and the small size (variety minor). Traditional healers commonly use the small size variety as contraceptive and this has been scientifically confirmed(1,4,5). The African Pharmacopoeia (1985) describes the seeds of *R. communis* as having slight irritating odour and a weak acid taste. The seeds are round, oblong and some what flattened, from 8 to 12mm long, 6 to 9mm wide and 4 to 8mm thick. The seed coat is brittle with a large yellowish endosperm(8). Microscopically, the seeds indicate that the epidermis consist of polygonal and pitted cells some with and others without brown contents. The palisade layer of seeds consist of brown, pitted sclerenchymatous cells, the large aleurone grains of the endosperm and the abundant fixed oils. The aleurone grains are round and ovoid and measure up to about 20mm in diameter. Castor oil seeds contain from 45 to 55% fixed oil, about 20% of protein substances consisting of globulin, albumin, nuclealbumin, glycoprotein and ricin (a toxalbumin), an alkaloid ricinin and several enzymes(9). The Total Ash value of the minor variety was

established to be 3.5% for the endosperm¹⁰ and acid – insoluble ash of 1.80%, then water-soluble ash of 0.90%. The seeds contain essential amino acids in moderate quantities in addition to some non-essential amino acids. Bicarbonate, carbonate, chloride and sulphate ions were not detected in the ashes of the seeds. The phyto-chemical screening of the seeds indicated the presence of steroids and alkaloids but triterpenes, flavonoids and tannins were not detected⁽¹⁰⁾. The steroidal compounds in the seeds that are responsible for the contraceptive activity has not yet been isolated and identified. This work that needs to be done is in progress.

MECHANISM OF ACTION AND CONTRACEPTIVE EFFECT.

Okwuasaba et al, 1991 observed that the petroleum ether fraction of the seed extract (0.6g/kg) prevented nidation in rats and none of the treated rats delivered pups at term⁽⁴⁾. The normal gestation period of rats is 21–23 days and it was observed that the extract protected such rats from pregnancy for greater than three gestation periods (75–90 days). The effect of the extract was reported by these authors to be reversible and they noted that when all the mated animals delivered, there were no fetal abnormalities observed in the pups and that the extract did not possess any anti-estrogenic effect. Studies on volunteers administered 0.51gm of the seeds orally as a single dose

gave protection against pregnancy for a sample of 50 women for a period of 12 months. Contraceptive efficacy of 100% was demonstrated in this study and both physical and chemical observation revealed minimal side effects (mild headache in some patients) and high compliance rate⁵. It is possible that the seeds may act by interfering with the process of fertilization and implanting into the uterus because substances having anti-fertility properties exert their effects at the ovarian level by inhibiting ovulation and/or steroid genesis. Since successful implantation depends on the correct timing in the menstrual cycle of the arrival of the blastocyst in the uterus, and couple with the fact that the extract does not inhibit regular oestrous in rats, disturbance of tubal transport may be responsible for failure of implantation. Accelerated transport of ova also result in a reduction in fertility, either through expulsion of the fertilized ova from the reproductive track or through degeneration of fertilized ova that arrive (too early) in the non-receptive uterus⁽¹¹⁾. Estrogen also accelerates the passage of ova through the uterine tubes and the uterus resulting in premature expulsion of ova from the uterus⁽¹²⁾.

FORMULATION STUDIES. Ripe castor oil seeds used by traditional medicine

practitioners as contraceptive medicine were used for the study reported in this review. The seeds were decoated, ground and prepared into granules (a form that improve flowability, compressibility and handling). The granules were subjected to pharmaceutical characterization by the determination of average granule size, friability, flow rate, angle of repose, bulk density, tapped density, percentage compressibility, moisture content, true density and porosity. These tests, which determines the quality of the granules indicated that the prepared granules were of good quality and can be used to produce good pharmaceutical dosage forms¹³. The granules were formulated into tablet using four different pressure levels, then, also formulated into capsule forms. These dosage forms were subjected to pharmaceutical characterization using tests which included hardness test, friability, disintegration test and tensile strength. The result indicated that these dosage forms were of good quality compared to some commercial tablets used as control⁽¹³⁾. The excipients used for the formulation of the granules were lactose, maize starch and methylcellulose as diluents then polyvinyl pyrrolidone (PVP) solution 5%, starch mucilage 10%, gelatin solution 10% and water as the binding medium or binder. The concentrations of the diluents were varied while the properties of the produced

granules and tablets studied to know which batches produced the quality granules and tablets. The best batch was used to determine the contraceptive activity of the dosage forms. The contraceptive efficacy of these dosage forms was determined using female albino rats. The results showed that these dosage forms had 80-100% contraceptive activity depending principally on the dose administered(13).

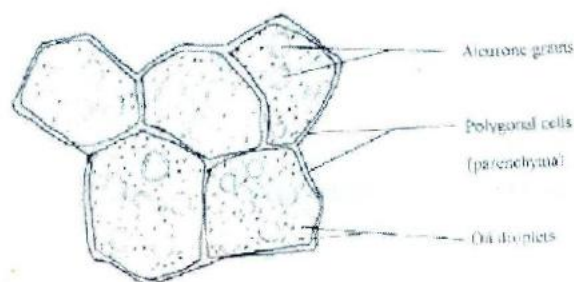
The formulation studies resulted in the production of two oral dosage forms, tablets and capsules, which revealed that lactose at 75% was the best diluent and when formulated with starch mucilage 10% as binder it produced the most durable elegant tablets. Analysis of the compaction behaviour of the granulation generally showed that the presence of the drug affected the compaction behaviour of diluents, altering their usual compaction behaviour. It was also observed that the presence of the drug reduced the tensile strength of the formulation significantly. The compacts generally exhibited type A and type B behaviour in Heckel's classification(13).

SAFETY AND CONTRA INDICATION

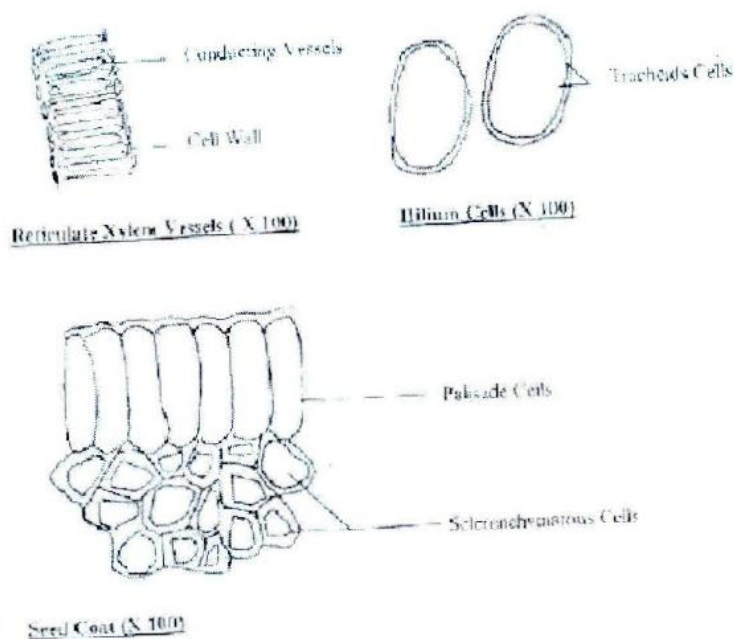
Since vast majority of contraceptive drugs are metabolized in the liver through biochemical process of ring reduction, in-activation and conjugation for final elimination through the bile and kidney it is necessary to look at the effect of this drug on these organs. A

study by Das S.C. et al, 1997 indicate that the extract (diethyl ether) of the seeds of *R.communis* Linn had no effect on the serum parameters of renal functions in albino rats. These authors also administered the dried seeds orally to human volunteers then studied the effect on the liver and kidney function. Their results demonstrate that the seeds of *R.communis* Linn had no effect on the function of the liver and kidney if taken at the therapeutic recommended dose (0.51 gm) per patient. Comparison of the mean values of serum parameters of the liver and kidney of the treated albino rats and the control indicated no significant difference ($P<0.05$)(14). The result therefore showed that the integrity of the liver was not affected as determined by the values of alkaline phosphate, transaminase, transpeptidase, protein, albumin and bilirubin in volunteers. The values were within the normal range after single administration of the therapeutic dose. Renal function was not significantly impaired in the volunteers after the administration of the drug ($P<0.05$). This study demonstrated that the high

compliance and acceptability might be due in part to the absence and/or minimal side effects particularly, headache, nausea, weight gain and increased blood pressure noticed on a few number of the volunteers. This therefore indicated that over the observed period of 12 months, the renal and liver function were unimpaired. In addition the study showed that the serum lipid profile was not significantly affected. When all these effects are considered together, it is not unreasonable to suggest that *R. communis* Linn. variety minor possesses a unique antifertility and contraceptive property different from the hormonal contraceptives and represents a significant break through in family planning biotechnology. Acute Toxicity studies were also reported to determine the LD50 of the extract of the seeds of *R. communis* Linn. Results indicated that the LD50 was 13.17 gm/kg, which means that the extract has a wide margin of safety¹³. The drug, which should be indicated for matured women, is contra-indicated for men, children and it should be avoided in patients with impaired liver and kidney function.



Endospermous Cells (X 400)



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