Male contraceptive pills

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ABSTRACT

The benefits and drawbacks of vasectomies and condoms will be covered in this study on male contraceptive tablets before a discussion of the research on new male contraceptive techniques.
A novel male contraceptive could work in one of the following three ways:

1. By employing a physical barrier, such as a condom, to block the flow of sperm to the egg, or by surgically occluding the vas deferens or utilising another vas occlusion technique.
2. By totally stopping sperm production.
3. By killing the sperm or inhibiting an essential sperm function (e.g., sperm motility) either before ejaculation or inside the female reproductive tract.

No androgenic contraceptive has been described that induces azoospermia in all men. Oral testosterone is rapidly broken down in the liver, so oral administration of testosterone is ineffective. Consequently, long-acting testosterone esters like those found in most androgenic contraceptive regimens: B. Testosterone enanthate administered weekly by intramuscular injection.Recent male contraceptive research has combined progestin and testosterone. Progestin also suppresses her LH and FSH secretion from the pituitary gland. However, the contraceptive efficacy reported in this study was low, with several couples becoming pregnant during treatment.

Key words: *contraceptives, hormonal, non-hormonal, pills, drugs.*

I: INTRODUCTION

1.1 Definition of contraceptive:

The definition of “contraception” the purposeful rejection of conception with the use of different devices, sexual behaviors, chemicals, medications, or surgical treatments is known as contraception. As a result, a contraceptive can be any tool or action that prevents a woman from getting pregnant [21]. Women are primarily responsible for preventing pregnancy since they have access to a wide range of birth control methods, such as tablets, patches, and intrauterine devices. [16]. Male condoms and vasectomy are the only two alternatives available to men both of which have significant limitations [1]. Despite the social need and willingness of men involve or participate in family planning, to date there are no male contraceptives available in clinical use. Vasectomy and male condoms are the only two male contraceptive methods currently available, both of which have significant limitations [2]. On the other hand, non-hormonal methods of contraception are the most promising research area in MCM, as they can be highly specific, at least in theory. However, more of them are still experimental or have long been abandoned due to toxicity. Therefore, until reliable, safe and practical male contraception is developed, most of the contraceptive burden will have to be borne by women [2]. Oral contraceptives are especially popular due to their convenience and non-invasiveness. But since they are currently only available to women, the question arises: Where are the pills for men? However, they often encounter undesirable but common problems: testicular shrinkage. There are reports of potential oral hormone pills for men, but many such as increase in weight and loss of libido. There are still side effects of Therefore, the male oral drug market is still very scarce and untapped [8]. About 40% of pregnancies are unplanned. This is because society has misdirected women as primarily responsible for contraception and family planning. In the past, male contraceptive options were suboptimal [15].

- Condoms (not always safe)
- The withdrawal technique (ineffective)
- Vasectomy (potentially irreversible)

1.2 Advantages of contraceptives pills:

- Studies have shown that family planning, including planning, delaying and spacing pregnancies, either directly or through healthy maternal behaviour during pregnancy, is associated with improved birth outcomes for babies.
- Birth control methods have many benefits in addition to their primary purpose of preventing pregnancy Contraception decreases pregnancy-related ailment and mortality, lowers the risk of certain reproductive cancers, and can be used to cure many menstrual symptoms and disorders.
- Including contraception, many other useful healthcare prevent, test, and men and women who see their doctor can receive treatment for diseases and conditions like gonorrhoea, HIV, HPV, cervical cancer, and chlamydia. They can also receive treatment to prevent intimate partner violence.
- As not all females have same access to the many advantages of contraception and other health services, additional efforts are needed to increase access to contraception and implement programs and policies that improve health outcomes for all women. [19].
- Affordable and simple to use. without any harmful side effects. Simple to obtain. Reversible [11].

The science of male birth control is tricky, too. A pill needs to do at least one of a few things for it to be effective, according to researchers:
- Reduce or halt the production and development of sperm
- impede the sperm's exit from the body
- To prevent the sperm from reaching their intended location, slow them down. - Prevent the egg from being fertilized by sperm. [11]

II: MOST COMMONLY USED METHODS

2.1. Existing contraceptives

2.1.1 Condoms:

Male condom: It's a physical blocking method of contraception. A condom is a small, loose-fitting sac or sheath used to prevent sexually transmitted infections and illnesses (STIs). Condoms serve as a barrier method of contraception, preventing conception by preventing semen, a fluid containing sperm, from entering the vagina and fertilizing the eggs [20]. With few adverse effects, condoms offer safe, affordable, accessible, user controlled contraception. If a person has a latex allergy, non-rubber condoms (made of polyurethane or a natural membrane) can be used instead [6].

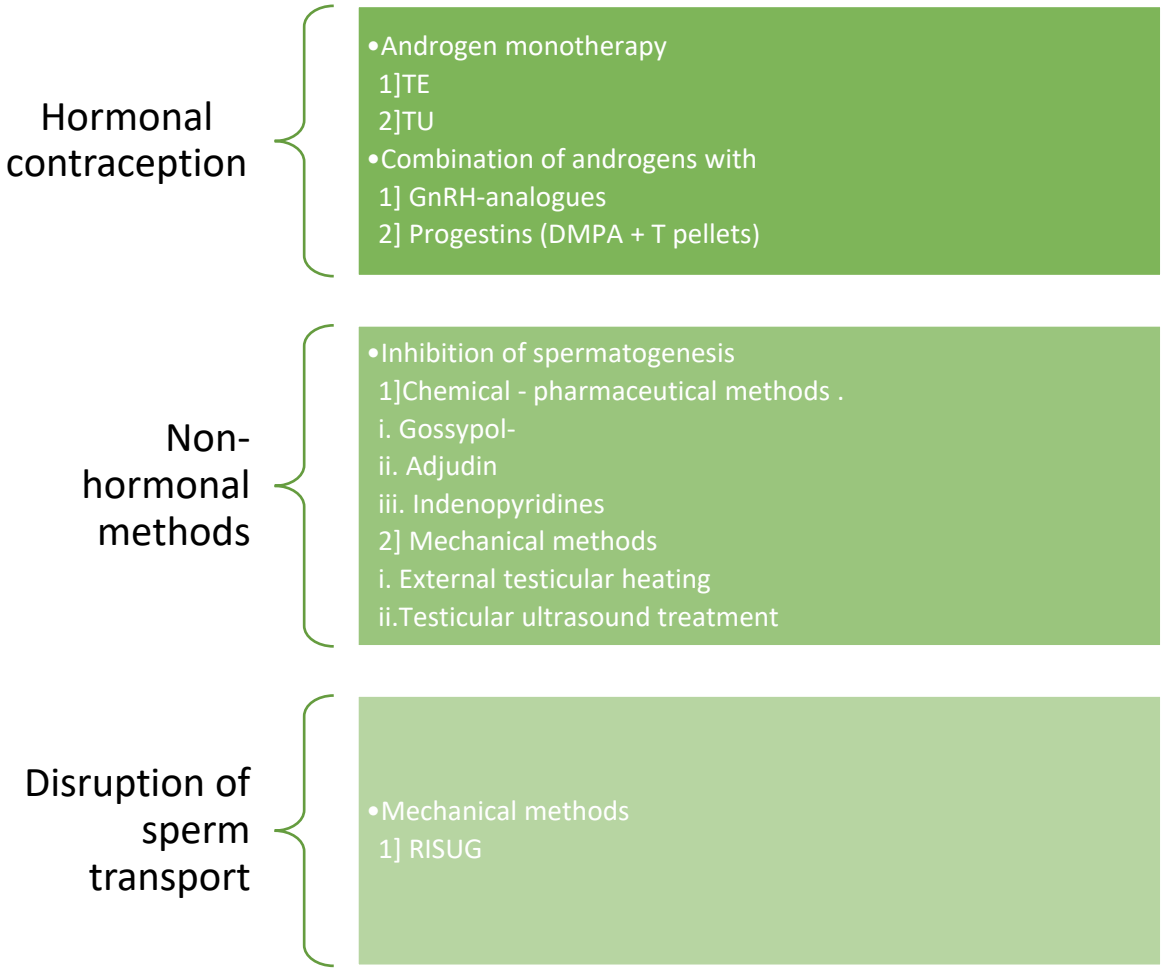
2.1.2 Vasectomy:

The name of the tubes in your scrotum that are blocked during the procedure is where the word "vasectomy" originates: Vas deferens [22].Only 2.4% of men worldwide use the vasectomy as a highly effective and secure method of contraception for couples who want to stop having children [23].

- **One of the following three methods could explain how a novel male contraceptive function:**

1. By employing a physical barrier, such as a condom, to block the flow of sperm to the egg, or by surgically occluding the vas deferens or utilizing another vas occlusion technique.
2. By blocking spermatogenesis entirely.
3. By eliminating the sperm or preventing it from performing a crucial sperm function (like motility), either prior to ejaculation or while it is inside the female reproductive system [3].

III: CONTRACEPTION METHODS UNDER INVESTIGATION



3.1 Contraception methods under investigation:

3.1.1] HORMONAL APPROACH TO MALE CONTRACEPTION [3]

Hormonal targets for contraception have evolved over the last 40 years. Androgenic contraception aims to induce suppression of spermatogenesis through hormone replacement. Infertility thus produced must be reversible. To achieve the desired oligospermia or azoospermia, in addition to suppressing FSH, testicular testosterone levels must be lowered. Such a drop in testicular testosterone levels can lead to symptoms of hypogonadism that require external testosterone replacement. Suppression of pituitary gonadotropins and cessation of spermatogenesis can be achieved by testosterone injection alone. But the problem here is that his one-third of patients who may need additional drugs may not be properly suppressing spermatogenesis. Clinical research in the field of androgenic contraception has been conducted over the past 50 years. However, many studies had their own limitations. The 10th Androgenic Contraceptives Summit proposed that for regulatory approval of androgenic contraceptives, clinical trials must meet the following criteria:

1. A Phase II dose-ranging study may use suppression of spermatogenesis as the main parameter. Sperm concentration can be used as a surrogate metric; the objective should be ≤ 1 million/ml and should be measured using the World Health Organization's recommended method.
2. Each individual should be monitored until spermatogenesis is shown to be flexible enough to meet criteria compatible with normal fertility when therapy is stopped. Regaining sperm concentrations between 15 and 20 million/mL typically shows sufficient signs of viability. These figures will probably decline as more information on pregnancy-related characteristics becomes available.

3. Men are only now permitted to take part if their sperm levels are approximately 20 million/mL. This obstacle may potentially be removed if more information regarding fertility parameters becomes available. Participants in clinical efficacy trials who know or suspect they are infertile should not be used.
4. If the primary endpoint of an open-label, non-comparative contraceptive efficacy trial is not likely to be biased, then it is appropriate.
5. Two non-dependent phase III trials were conducted to assess the effectiveness of contraception, lasting a year after male subjects' sperm counts were lowered to less than 1 million/mL .
6. The experiment should involve at least 300–600 men in the desired combination and dose for six months, 100 for a year, and a total of 1500 men in Phase I to be included in phase III studies, in order to guarantee the safety of the new chemical.
7. Post-market surveillance to ensure continued safety over time.
8. The necessary laboratory tests, particularly the examination of sperm, must to be carried out under stringent quality control.

A study of the efficacy of hormonal contraceptives in men showed an overall efficacy of approximately 95% when the sperm count decreased to below 1-5 million sperm/ml. Sperm concentrations below 1 million sperm/ml semen were associated with a pregnancy risk of approximately 1%. The next section provides an overview of the most important clinical studies on hormonal contraception [3]. Oral testosterone administration is unsuccessful since the liver breaks down oral testosterone so quickly. Therefore, long-acting testosterone esters have been used in the majority of male hormonal contraception regimens. [5].

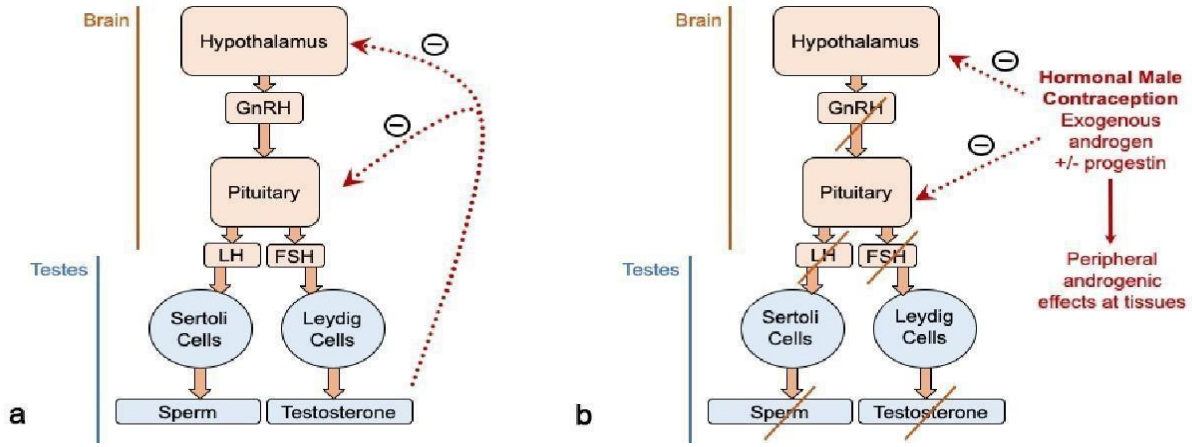


Figure 3.1. Mechanism of Hormonal Male Contraception.

a. Hypothalamic-pituitary-gonadal axis in a normal male. The hypothalamus secretes, which stimulates the pituitary to release luteinizing hormone (LH) , follicle-stimulating hormone (FSH) and gonadotropin-releasing hormone (GnRH). FSH and LH stimulate Sertoli cells which leads to sperm production (spermatogenesis) and Leydig cells to promote testicular testosterone production. To complete the classic feedback loop, circulating testosterone inhibits her FSH, GnRH, and LH secretion.

b. Introduction of hormonal contraceptives (androgen +/- progestin) leads to suppression of circulating LH, GnRH, and FSH, resulting in suppression of testicular testosterone and spermatogenesis. Androgenic effects are maintained by peripheral effects of exogenous androgens on non-gonadal tissues [17].

a) Androgen monotherapy

- **Testosterone Enanthate [3].**

In an efficacy study conducted by the World Health Organization (WHO), healthy men were given 200 mg testosterone enanthate (TE) weekly IM for 6 months. The study team included both Asian and Caucasian men. After a median of 4 months, 65% of males started to lose their ability to reproduce. According to the study, he had a success rate of more than 99% and a pregnancy rate of 0.8 per 100 person-years. We were unable to evaluate the regimen's actual efficacy since only males who were azoospermic were allowed to enter the efficacy phase. Following the first research's limitations, WHO planned a second multicenter investigation. According to this study, 8.1 conceptions per 100 person-years (3 million to less than 5 million/ml) were the lowest fertility rate among guys with low sperm concentration. Although these studies showed fairly good efficacy, they also had some drawbacks. One, of course, was the

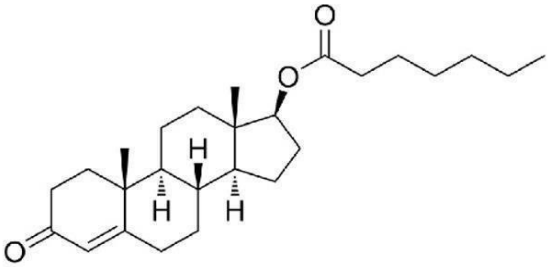


Fig.3.2. Testosterone Enanthate

requirement for weekly intramuscular injections, as well as a reversible reduction of volume in testicular, increase in haemoglobin by 6% and 10-15% decrease in HDL cholesterol levels. There was also a delay of 3-4 months before the full contraceptive effect was achieved. However, quality of life and sexual function remained good.

- **Testosterone undecanoate [3].**

Both oral and injectable forms of testosterone undecanoate are offered. Chinese men received injections of 500 mg or 1000 mg of testosterone undecanoate monthly for the first research. Not only did everyone in the 1000 mg group develop azoospermia, but they did so more quickly than the 500 mg group did. However, the Caucasian population did not have a similar level of effectiveness to that of the Asian group. Another think about from China proposed a month to month testosterone undecanoate stacking dosage of
1000 mg and 500 mg. An assist infusion convention was attempted. Men were fair 3 percent incapable to preserve sperm concentrations underneath 3 million/milliliter. The viability of contraception was 96.7%. Six men did, be that as it may, involvement sperm bounce back amid the legitimacy period. Utilizing testosterone undecanoate once more, a later Chinese consider uncovered a pregnancy rate of fair 1.1/100 person-years.

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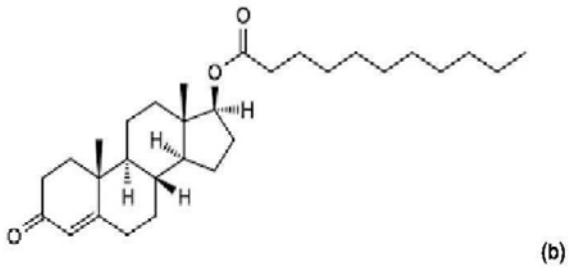

Fig.3.3 Testosterone undecanoate

b) Combination of androgens with

- **Gonadotropin-releasing hormone-based contraceptive therapy [3].**

One of the most essential tasks of FSH and testosterone is to maintain spermatogenic homeostasis by blocking death signs for germ cell antagonists, which have been used as an adjuvant in androgen therapy for male birth control. In a trial using Nal-Glu in combination with TE, azoospermia was induced at 12 weeks and was then maintained by TE alone for 20 further weeks, showing a role in azoospermia induction. When the GnRH antagonist cetrorelix was combined with 19nortestosterone, azoospermia increased in all participants, but it was no longer maintained once cetrorelix was discontinued. It's probable that because a non-aromatizable androgen was used, the estrogen-pituitary feed-back suppression that had previously existed was lost, failing to inhibit spermatogenesis. In a combination study, acyline mixed with DMPA and testosterone gel showed no significant difference in sperm suppression or sperm suppression speed compared to testosterone and DMPA alone. More research is needed to clarify the effects of GnRH antagonists on birth control before they can be used scientifically. GnRH agonists are rarely utilized since they allow for continuous FSH production.

- **Progestins (DMPA + T pellets) [3].**

It has been demonstrated that progestogen and testosterone combination therapy is more effective than testosterone monotherapy at inhibiting spermatogenesis. This is because progestogens have the ability to prevent the pituitary gland from secreting gonadotropin. An RCT comparing the two therapies indicated that levonorgestrel plus TE was more effective in producing azoospermia than TE alone. Furthermore, there is no proof that testosterone undecanoate and norethisterone together significantly increase azoospermia. Research from Australia and China have shown that combining DMPA and testosterone produces positive results. One disadvantage of this treatment is that it requires more injections. Castor oil can be used to dissolve testosterone undecanoate and 19-norethisterone enanthate, which can subsequently be administered simultaneously. However, research results on this combination are still pending. Significant concerns for concern include the significant decline in HDL cholesterol and the weight gain linked to progesterone and testosterone together. As a result, efforts are concentrated on minimizing these adverse effects. Patients received subcutaneous injections of testosterone pellets and etonogestrel implants, which was demonstrated to produce significant rates of azoospermia. It's interesting to see that less HDL cholesterol was reduced when the progestogen route and type were changed. Another trial included etonogestrel and 750–1000 mg of testosterone undecanoate every 10–12 weeks. 90% of patients had spermatogenesis below 1 million/mL, which was decreased. All androgenbased therapies have been demonstrated to carry a small risk of benign prostatic hyperplasia, or prostate cancer, which will be randomly assessed.

3.1.2] Non-hormonal methods [16]

Women are largely responsible for avoiding pregnancy since they have access to a wide variety of contraceptive methods, including tablets, patches, and IUDs. However, there may soon be more options for male contraception and associated responsibilities. Scientists have recently reported on a nonhormonal male contraceptive that prevents pregnancy in mice and doesn't seem to have any detrimental side effects. Reversible, long-lasting, and dependable contraceptives are necessary for men. To develop a non-hormonal method of male contraception, researchers concentrated on the protein known as retinoic acid receptor alpha (RAR-). This protein belongs to a family of three nuclear receptors that bind retinoic acid, a derivative of vitamin A that is essential for the development of embryos and cells. Knocking out

RAR-α gene in male mice renders them sterile with no apparent side effects. Other researchers have created an oral substance that suppresses all three RAR family members (RAR-α, -β, and -γ) and renders male mice infertile. RAR for research We examined the crystal structures of -α, β,and -γ receptors bound to retinoic acid and discovered structural variations in the three receptors' interactions with the same ligands. Armed with this knowledge, they created and produced about 100 chemicals, then tested how well they could specifically block RAR- in cells.. They identified a compound called YCT529 that inhibited RAR-α nearly 500 times more potent than RAR-β and RAR-γ. When administered orally to a male mouse for time of 3 4 weeks, YCT529 vividly condensed sperm count and prevented him from becoming pregnant by 99% with no observable side effects. Mice were able to reproduce 4-6 weeks after discontinuing the compound[16].

a) Inhibition of spermatogenesis [3].

- **Chemical - pharmaceutical methods**

i. Gossypol [3].

An fascinating plant extract made from cotton is called gossypol. Both spermatogenesis and sperm motility were found to be impacted by it. Research on gossypol has mostly been done on Chinese men. The majority of users were able to successfully lower sperm concentrations to those needed for contraception. However, at least one-fifth of the patients experienced an irreversible consequence. Hypokalemia and sporadic paralysis were two additional significant dose-dependent adverse events.

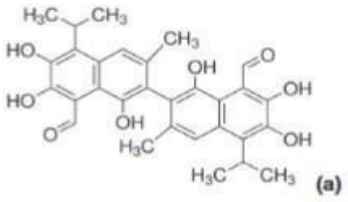

Fig.3.4 Gossypol

ii. Adjudin [3].

A derivative of lonidamine called adjuvant was developed as an anticancer drug. It has been shown that adjuvants interfere with sertoli cells' ability to adhere to germ cells. Within a week of starting treatment, spherical spermatids and spermatocytes were separated. The cytoplasm of Sertoli cells retracted, large vacuoles were formed, multinucleated germ cells were present, and the Sertoli cell nuclei were shifted to a higher location within the seminiferous epithelium, among other noteworthy changes. Adjudicated male rats exhibited inflammation of the liver and loss of skeletal muscle. An attempt was made to combine adjudin with recombinant mutant follicle stimulating hormone (FSH) protein, enabling testesspecific administration, in order to prevent these negative effects. The overall level of medication exposure was minimal, but the infertility induction was successful.

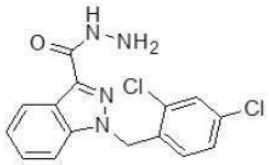

Fig.3.5 Adjudin

iii. Indenopyridines [3].

Indenopyridines are a class of investigational compounds that possess the capacity to modify Sertoli and germ cells. Sertoli cells may die as a result of indenopyridine lCDB-4022's disruption of Sertoli cell microtubule structure, activation of the ERK/MAPK (mitogenactivated protein kinase) pathway, inhibition of prosurvival factor expression, alteration of Sertoli-germ cell adherens junction protein expression, and induction of the proapoptotic factor Fa. Male rats developed reversible infertility when a gonadotropin-releasing hormone (GnRH) antagonist was present. When the medication was given to monkeys, sex steroid & gonadotropin concentrations remained unchanged, and no discernible toxicities occurred.

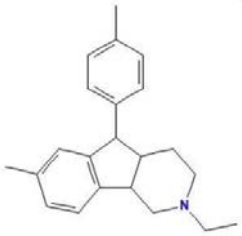

Fig.3.6 Indenopyridin es

- **Mechanical methods**

i. External testicular heating [3].

The testes have a lower temperature because to their extra intestinal position in the scrotum. It has actually been demonstrated that abruptly raising the temperature near the testes and scrotum lowers sperm concentration and results in infertility.

In a clinical investigation, testosterone combined with scrotal exposure to a hot water bath reduced sperm count and motility. In a clinical investigation, tight scrotal support also shown a reversible drop in sperm count.

ii. Testicular ultrasound treatment [6].

German scientist Rebecca Weiss won the James Dyson Prize last fall for inventing an "ultrasound-based, reversible, hormone-free" male contraceptive method. Before intercourse, the user simply inserts the testicles into a specially adapted device filled with heated water and the ultrasound temporarily stops sperm motility and prevents egg fertilization.

3.1.3] Interfere with the movement of sperm

a) **Mechanical methods**

Reversible inhibition of sperm under guidance (RISUG) [3].

With the help of Guha, reversible inhibition of sperm below guidance (RISUG) changed and evolved, and it has been the subject of research in India for a long time. A polymer of styrene maleic anhydride complexed with the solvent dimethyl sulfoxide makes up RISUG, which is injected into the vas using a no-scalpel technique. It is developing as a chance to have a vasectomy. After a few minutes after injection, RISUG hardens and sticks to the microscopic folds of the internal vas deferens partitions, preventing sperm from moving. The combination of fine and poor fees at the polymer floor causes the sperm membrane to be below ionic stress as soon as the sperm comes into contact with the polymer, which ultimately causes the sperm membranes to burst. A faster commencement of movement and the absence of granuloma development or autoimmune side effects are the advantages of RISUG over vasectomy. Although the method has shown to be beneficial, some patients have had reversible testicular swelling. More evidence is needed, despite some study showing that how RISUG is reversible. RISUG is now conducting medical trials below the Vasal gel call in the United States.

IV: OTHER DRUGS

1. **Tryptonide [7].**

This compound is a tryptonide and can be refined from an herbal medicine called Tripterygium Wilfordii Hook F or made by chemical synthesis.Oral administration of tryptonide once daily induces altered sperm with little or no motility, with nearly 100% penetrance, resulting in male infertility at 3–4 and 5–6 weeks. increase. When treatment is discontinued, males may become fertile again in about 4-6 weeks and produce healthy offspring. Short-term or long-term treatment with tryptonide had no discernible toxic effects. The bioavailability, effectiveness, reversibility, and safety standards for a strong contraceptive candidate appear to be all met by tryptonide. This makes it a promising male contraceptive for men that is not hormonal. suggests that tryptonide affects one of the final spermatogenic stages, altering sperm production and preventing it from developing the high motility needed for fertilization [7].

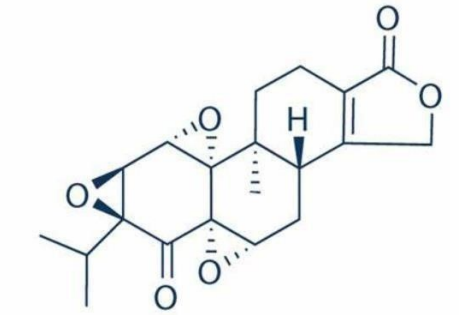

Fig.4.1 Tryptonide

2. **Nestron® (NES) [9].**

A daily gel including progestogen Nestron® (NES) and testosterone is part of another therapeutic regimen under development. Using T gel (100 mg) and NES gel (8 mg) lowered the concentration of sperm to 1 IU/L after 4 weeks of treatment in a proof-of-concept research. This allowed for a 97% sensitive prediction of treatment failure (sperm concentration >1 million/mL). Most failures were due to product mismatch or non-use, rather than failure to respond to medication regimens. When asked about their acceptance of the regimen, more than half of the participants said they were satisfied or very satisfied with the method. As part of the NICHD Contraceptive Clinical Trials Network, a contraceptive efficacy study evaluating her NES/T combined in one gel formulation for use as the primary contraceptive method in couples is ongoing [9].Nestrone acetate, or NES, is a progestin produced from 19-norprogesterone that is distinguished by the lack of androgenic, estrogenic, or glucocorticoid properties. It provides gonadotropin inhibition through a horrible feedback system, but it also prevents localised testosterone production from occurring right inside the testis. Testosterone gel may be used collectively with NES gel. This mixture used every day has proven powerful gonadotropin Suppression [18].

3. Dimethandrolone undecanoate (DMAU)

It is a once-daily tablet that inhibits two male sex hormones, luteinizing hormone (LH) and folliclestimulating hormone (FSH), and simultaneously reduces testosterone and sperm production [15]. The next step in DMAU research is to determine whether DMAU actually terminates sperm production Early data suggest that it is possible. The body produces sperm for about three months, so longer tests are required to determine whether sperm production can be completely stopped. [15]. In preclinical research, dimethandrolone undecanoate (DMAU) was found to have both androgenic and pregestational action.. It was shown that a single dose of up to 400 mg per day was safe, well-tolerated, and capable of lowering blood levels of FSH, LH, and testosterone to those linked to efficient contraception.

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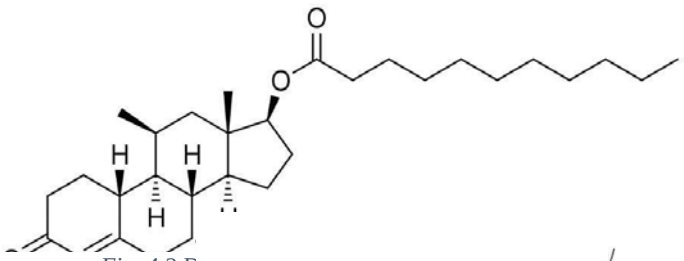

Fig. 4.2 D

4. 11-ßMNTDC

Another novel chemical is 11-beta-methyl19nortestosterone 17-beta-dodecylcarbonate (11- ßMNTDC), a 19-nortestosterone derivative. It suppressed serum gonadotropins in preclinical data, 30 and one trial in males found that given in oral doses of 100-800 mg with food, it is well tolerated and capable of suppressing testosterone[18].

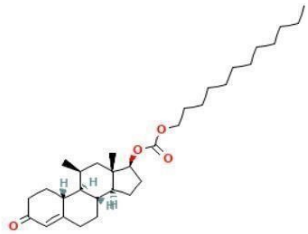

Fig.4.3.11-ßMNTDC

V: CLINICAL TRIALS & DRUG STUDIES

"Safety is very important for oral contraceptives because people are not taking them because they are sick, so they are less tolerant of side effects," says Noman. He and his colleagues found that when male mice were given a molecule, he called YCT529 a day for four weeks, sperm counts dropped sharply. Four to six weeks after the mice stopped treatment, they were able to reproduce normally again without any visible side effects [4].

Phase 1 Results with DMAU and MNTDC

Phase 1 studies suggested that each of the drugs may provide enough hormone suppression to lower sperm counts without causing significant hypogonadism symptoms. To put this potential to the test, each was subjected to dose-ranging phase 1 trials with a testosterone suppression endpoint. In the two placebo-controlled phase 1a studies, healthy male volunteers were randomised to receive two pills of active medication, four pills of active therapy, or a placebo.. In the combined study, 39 participants were given DMAU, 30 were given 11β-MNTDC, and 28 were given a placebo. The effectiveness was determined by monitoring testosterone levels. Patient questionnaires were used to assess tolerability. At the end of the 7 days, testosterone levels remained at baseline (400-600 ng/dl) in people receiving placebo. Score dropped to < 100ng/dL regardless of active ingredient or dose. Although both Jacobson apparently maintained testosterone levels below 100 ng/dl from days 7 to 28, 200 mg daily achieved a lower median suppression of testosterone than 400 mg daily (92.7 ng/dL vs. 49.6 ng/dL; P0.001). It didn't seem to matter how much testosterone was suppressed because tolerability was unaffected. The 4,444 subjects who took four and two pills a day "reported no significant differences in overall satisfaction or willingness to use the pill in the future or recommend it to other men," Jacob said and presented p-values for these results. It was not significant and ranged from 0.48 to 0.85. Overall, no serious adverse events occurred. Mild side effects related to hypogonadism occurred, but "were all resolved by the end of the study," she said [12].

- **DRUG STUDIES**

The second WHO study of male hormonal contraceptives examined the contraceptive efficacy of ET injections in men with tinea pedis or aggravated by ET injections. Similar to the prior WHO investigation, no male pregnancies resulted in roundworm births. Fertility was decreased to 8 pregnancies per 100 person-years in men who had few pregnancies. This translates to a contraceptive efficacy rate of 96.6% overall or a failure rate of 3.4%. After receiving the injections, all the males resumed normal spermatogenesis and experienced no negative side effects [13]. Weekly intramuscular testosterone injections are an effective

method of contraception for the majority of males, according to two WHO research. Nevertheless, a small proportion of men are unable to effectively control their sperm production and are consequently fertile. The substantial decrease in serum high-density lipoprotein (HDL) cholesterol, which might hasten the onset of atherosclerosis, is one of the diet's drawbacks. has been used to treat male hypogonadism for the past ten years. TU injection normalized serum T levels in men with hypogonadism at 6-12 weeks. In China, two significant TU injectable male hormonal contraceptive trials were carried out in the late 1990s and early 2000s. During the induction period, a monthly injection of 500 or 1000 mg TU is administered. The remaining 95% of these males had semen with less than 1 million sperm per milliliter. Then, for a year, these men relied solely on the injection to prevent pregnancy. There was just one pregnancy reported, and overall effectiveness was around 95%. A second study, which included more than 1,000 men, found a 94% overall success rate for contraception. A 7% rise in hematocrit and a 23% increase in HDL cholesterol were among the adverse events in these studies, although neither of these changes led to subject cessation, and no significant adverse events were noted. The approach hasn't been licenced for clinical use by China's pharmaceutical regulatory authorities despite these encouraging results for an unidentified reason. More recent investigations of male contraceptives have coupled progestin with testosterone in an effort to achieve 100% azoospermia in males undergoing hormonal contraceptive trials. The action of progestin is to prevent the pituitary gland from secreting FSH and LH. However, the study's stated contraceptive efficacy was weak, with some couples getting pregnant while receiving the medication. [13].

- **Study of Tryptonide**

Scientists from China and the United States recently claimed that they have found chemicals that, as opposed to totally blocking sperm production in mice and monkeys, inactivate sperm activity. Purified tryptonide was obtained from Tripterygium Wilfordii Hook F, a Chinese herb that has been demonstrated to induce infertility in patients. Tryptonide was shown to cause sperm to distort and lose their function in mice and monkeys. Months may pass before the animals experience any toxicity or negative effects from this effect. Crucially, the effect may be reversed. It took many weeks for the animals' fertility to return after they stopped consuming the chemical. Tryptonide's potential as a male contraceptive option was therefore demonstrated by its effective, reversible, and non-toxic capacity to convert and inactivate sperm. Next, the researchers tried to figure out how tryptonide rendered sperm inactive [8]. When the substance was examined to see if it could attach to every protein in the mouse testicles, they discovered that tryptonide could attach to a protein known as junction plakoglobin (JUP). JUP is a protein that participates in spermatogenesis, the last stage of sperm development, and works in concert with other critical proteins in sperm. As a result, binding to JUP causes abnormalities in the final sperm cells that are generated, as well as disrupting the function of other critical proteins throughout sperm formation. Overall, tryptonide was shown in this study to be a viable option for male contraception. The results in this publication were helpful in validating methods that use male contraceptives to inhibit sperm production, even though they were not examined in the study. This could broaden the field of male oral contraceptive research and development.Potential male oral pill candidates could lead to more equitable times in the future.

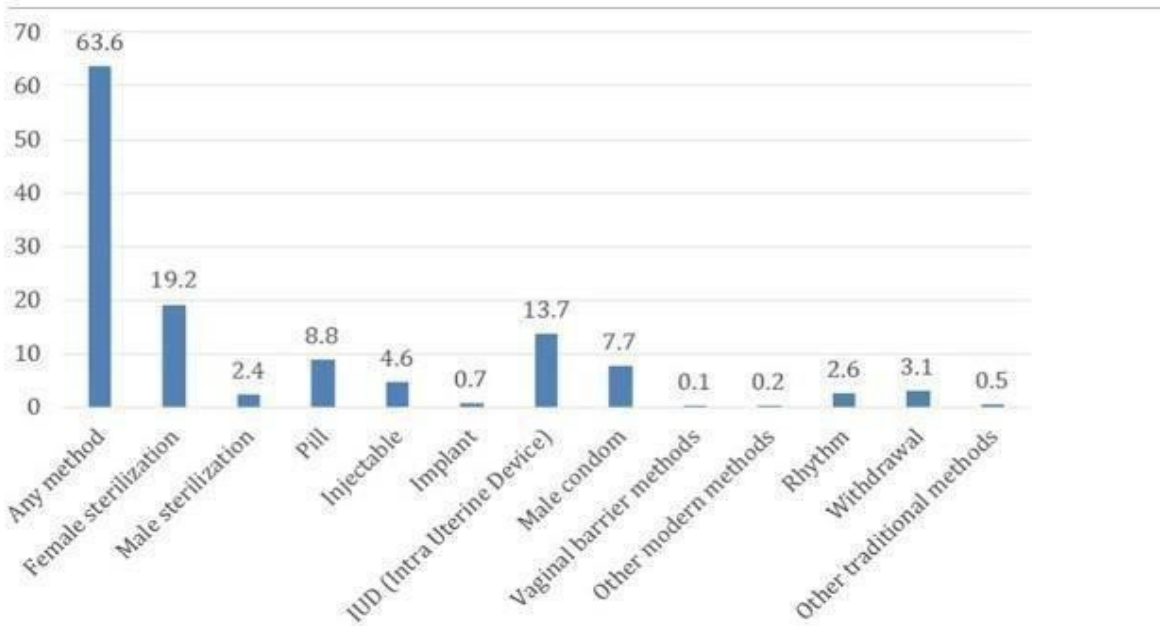

Fig.5.1 Estimates of contraceptive prevalence by method among married or in-union women aged 15 to 49(percentage)[14].

Table.5.1 Male hormonal contraceptive efficacy trials [9].

Regimen	N enrolled	N entering/ completing efficacy	Pregnancy/failure rate per 100 couple years	Author / Sponsors
Testosterone enanthate weekly injection	271	157/119	1 0.8(0.0 to 4.5)	WHO 1990
Testosterone enanthate weekly injection	357	268/209	4 1.4(0.4 to 3.7)	WHO 1996
Testosterone undecanoate injection + norethisterone enante injection every 8 weeks	320	266/111	4 2.2 (0.8 to 5.8)	WHO/CONRAD; Behre et al.2016
Testosterone implant every 4-6 months + depomedroxyprogesterone acetate injection q 3 months	55	53/28	0 0(0 to 8)	Turner et al. 2003
Testosterone undecanoate monthly injection	308	296/280	1 2.3 (0.5 to 4.2)	Gu et al. 2003
Testosterone undecanoate monthly injection	1045	855/733	9 1.1(0.4 to 1.8)	Gu et al. 2009
Testosteron +Nestorone transdermal gel applied daily	ongoing	ongoing	ongoing	NICHD

CONCLUSION

Many new methods as oral or transdermal hormones male contraceptives are still in development and have few side effects. Our future goal is to develop and commercialize a male contraceptive method that allows both men and women to play a major role in family planning. There are currently no non-hormonal male contraceptives available on the market, despite years of research into creating a "male pill." Even though men are eager and required by society to participate in family planning. There are no clinically effective male contraceptives on the market as of now. The only two male contraceptive options now on the market are vasectomy and male condoms, both of which have substantial drawbacks. The most commercialized product is MHC. Unfortunately, concerns regarding the impracticality of their use, unpredictable response rates, and associated long-term cardiovascular and prostate disease morbidity have drawn the pharmaceutical industry away from further research in this field. However, because non-hormonal methods of contraception can be exceedingly specific—at least in theory—this is the most potential area of MCM research. However, most of them have been abandoned due to toxicity for a long time or are still in the experimental stage. Consequently, until a reliable, secure, and useful form of male contraception is developed, women will have to bear the majority of the hardship associated with using contraception.

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