

Contraception: Herbal and Modern Strategies

NURUL AIN KB¹, IRFAN Y², MAHANEM MN¹

¹*School of Bioscience and Biotechnology, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, 43600 Bangi, Selangor, Malaysia.*

²*Department of Obstetrics and Gynaecology, School of Medicine, University of Otago, Christchurch, New Zealand.*

ABSTRAK

Ledakan penduduk merupakan salah satu isu global yang menjadi perhatian. Peningkatan bilangan penduduk turut menyumbang kepada kesan negatif terhadap sosial dan ekonomi. Untuk mengatasi masalah ini, kontrasepsi moden yang mudah dan selamat telah diperkenalkan. Walau bagaimanapun, kini, ramai penyelidik telah menjalankan kajian mengenai keberkesanan tumbuhan ubatan sebagai agen kontraseptif pada model manusia dan haiwan. Oleh itu, kajian mengenai kontraseptif herba dan moden telah dirumuskan dalam artikel ini. Sebanyak 66 artikel yang berkaitan telah didokumen mempunyai maklumat mengenai kontraseptif moden dan herba. Kesemua kontraseptif adalah berkesan dengan syarat digunakan secara konsisten dan cara yang betul. Kontrasepsi sangat penting kerana dapat mencegah penyakit dan jangkitan yang disebabkan oleh hubungan seksual dan menghalang kehamilan yang tidak diinginkan. Oleh itu, artikel ini merupakan usaha untuk meringkaskan potensi tumbuhan ubatan sebagai agen kontraseptif dan kaedah kontraseptif moden yang digunakan sebagai pencegahan kehamilan pada lelaki dan wanita.

Kata kunci: kontrasepsi, pencegahan kehamilan, tumbuhan ubatan

ABSTRACT

Population explosion is one of the global issues of concern. The increasing number of individuals could result in negative impact on social and economy. To overcome this problem, convenient and safe modern contraception was introduced. However, recently many researchers have conducted studies on the effectiveness of medicinal plants as contraceptive agents on human and animal models. Therefore, the studies of herbal and modern contraceptives were summarized in this review article. A total of 66 relevant articles were documented having

Address for correspondence and reprint requests: Assoc. Prof. Dr. Mahanem Mat Noor. School of Bioscience and Biotechnology, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, 43600 Bangi, Selangor, Malaysia. Tel: +603-89215193 Email: mahanem@ukm.edu.my

information regarding the modern and herbal contraceptives. All contraceptives are highly effective provided they are used consistently and in the proper way. Contraception is important as it could prevent diseases and infections caused by sexual intercourse and prevent unintended pregnancy. Therefore, this review is an attempt to summarize the potential of medicinal plants as contraceptive agents and the modern contraceptive methods used as birth control in males and females.

Keywords: birth control, contraception, medicinal plants

INTRODUCTION

The world population has been increasing for years and recently, the rate of increase is accelerating because majority of the people in the world comprise young generation, planning to have the first children. Few decades ago, we were warned of the dangers of overpopulation. In the early 1960s, severe famines in India and other parts of Asia had caused millions of death. Therefore, developing countries have been using various methods to control the size of population (Pei & Nai 1991). However, the world population could still increase despite the increasing availability of contraception. As reported by a previous study (WHO 2018), the use of contraceptives increased from 54.0% in 1990 to 57.4% in 2015 in many countries especially in Asia (60.9% to 61.8%), Latin America (66.7%) and Africa (23.6% to 28.5%). Some people claim that even through contraception could curb the growth of population, it could cause environmental disturbance, while few said that it is entirely altruistic to improve their quality of life. The choice of use contraceptives depends on many factors. However,

couples commonly use contraceptives to limit the size of their family. There are two types of contraceptives methods being discussed in the present review i.e. herbal and modern contraceptives. Previous researchers claimed the protective effect of herbs as contraceptive agent. The medicinal plants such as *Centella asiatica* (Yunianto et al. 2010; Mohamed et al. 2014; Yunianto et al. 2017), *Dendrophthoe falcate* (Gupta & Kacchawa 2007), *Andrographis paniculata* (Sakilah et al. 2009; Mohamed et al. 2014; Dayang & Mahanem 2015; Khaidatul & Mahanem 2017), *Azadirachta indica* (Bhasin et al. 2001; Kabeh & Jalingo 2007; Kumar et al. 2012; Das et al. 2014), *Carica papaya* (Lohiya & Goyal 1992; Udoh & Kehinde 1999; Udoh et al. 2005; Kamal & Gupta 2003; Christine & Mahanem 2012; Das et al. 2014; Julaeha et al. 2015) and *Momordica charantia* (Boetse et al. 2011; Yama et al. 2011; Mohamed et al. 2014; Adewale et al. 2014a; Adewale et al. 2014b; Tumkiratiwong et al. 2014) were widely used as contraceptive agents for males and females. Besides that, the modern contraceptives could be categorised into two types which were irreversible and reversible

contraceptives. The irreversible methods provide permanent contraception such as vasectomy (97% to 99%) and tubul ligation (99%). The reversible contraceptive methods mainly focus on barrier methods such as condom (79% to 98%), intrauterine device (99%), spermicides, cervical caps and diaphragms. The hormonal method consists of hormonal pills (90% to 99%), implants (99%) and injectable hormone (97% to 99%) (WHO 2018). Even so, contraception has many advantages in preventing sexual transmitted diseases including HIV/AIDS, reducing the number of infant mortality, and preventing unintended pregnancy among young adults. This study would help individuals with proper family planning as well as understanding various methods of contraception including medicinal plants and modern contraceptives.

MEDICINAL PLANTS AS CONTRACEPTIVE AGENTS

Herbs have been widely used throughout the world in preventing and treating various diseases. Recently, studies have proven that medicinal plants can be used as antifertility agents for males and females. They induce infertility in terms of antispermatogenic, anti-ovulation, and anti-implantation. Drugs that could control fertility (Kumar et al. 2012) are commonly referred as oral contraceptive. In male, the antifertility agents could disturb the production of male sex hormone which is testosterone, preventing spermatogenesis, and produce low sperm motility. While in females,

the antifertility agents could prevent ovulation, fertilization, and embryo implantation; some agents could also cause abortion. Medicinal plants that possess antifertility properties for male and female are shown in Table 1, Table 2 and Table 3.

Centella asiatica

Centella asiatica belongs to the family Apiaceae and subfamily of Hydrocotyloideae. It has been reported to show anti-inflammatory, antifertility, antispermatogenic and anti-implantation activities (Yunianto et al. 2010; Nurlaily et al. 2012; Yunianto et al. 2017). A previous study has used high dose of *Centella asiatica* (300 mg/kg) on 32 fertile male rats and it resulted in low sperm quality, low testosterone level, and altered the morphology of testicular cells (Yunianto et al. 2010). Moreover, female rats that mated with male rats, were treated with *Centella asiatica* and showed anti-implantation activity in which the number of implantation sites (100 ± 2.82) decreased compared to the normal group (183 ± 2.14) with the percentage of infertile male rats in the treated group being 43.75% and in the the control group, it was 18.75%. Sperm proteomic analysis was also carried out using MALDI-TOF. It was found that three interested protein spots (sorbitol dehydrogenase, glutamine synthetase, and lipocalin) in the treated group disappeared (Yunianto et al. 2017). Sorbitol dehydrogenase plays an important role in the energy production for spermatozoa and maturation of germinal epithelium (Pant et al. 1995;

Table 1: Antifertility agents extracted from plants for male

Botanical/Common name	Type of extraction	Part used	Action	References
Albizia lebeck (L.) (Siris, Woman's Tongue) Family: Fabaceae	Methanol extract	Pod, bark	Antispermato-genic Spermicidal activity	Gupta et al. 2004; Gupta et al. 2005
Barleria prionitis (Vagradanti,Vjradanti) Family: Acanthaceae	Methanol extract	Root	Antispermato-genic	Gupta et al. 2000; Singh & Gupta 2016; Verma et al. 2005
Carica papaya (Papaya, Papita, Hogegegulo) Family: Caricaceae	Chloroform extract, aqueous extract, alcohol extract	Seed, leaf	Antispermato-genic Spermicidal activity	Das et al. 2014; Julaeha et al. 2015; Christine & Mahanem 2012 Lohiya & Goyal 1992; Udoh & Kehinde 1999; Udoh et al. 2005; Kamal & Gupta 2003
Cannabis sativa (Ganja, Bhang) Family: Moraceae Cannabaceae	Alcohol extract	Root	Antispermato-genic	Mohamed et al. 2014; Joshi et al. 2011; Sailani & Moeini 2007
Dendrophthoe falcate Family: Loranthaceae	Methanol extract	Stem	Antispermato-genic	Gupta & Kacchawa 2007
Elettaria cardamomum (Queen of spice, Cardamomum) Family: Zingiberaceae	Aqueous extract	Seed	Spermicidal activity	Khillare & Singh 2014
Terminalia chebula (Chebulic myrobalan) Family: Combretaceae	Aqueous ethanol extract	Fruit	Antispermato-genic	Ghosh et al. 2015
Tripterygium wilfordii (Yellow vine root) Family: Celastraceae	Methanol, ethanol extract	Root xylem	Antispermato-genic	Kutney et al. 1992; Qian 1987

Pant et al. 2004). According to a previous study (Srivastava et al. 1990), low activity of sorbitol dehydrogenase could destruct the seminiferous tubule in the testis.

Andrographis paniculata

Andrographis paniculata is another herb that has been studied on animals and claimed to be a natural contraceptive agent. This plant with antispermato-genic activity belongs

to the family Acanthaceae which is commonly found in the South East Asia of China and India. It also has been widely used for treating HIV/AIDS and acts as an antidiabetic agent (Niranjan et al. 2010). A study was conducted to investigate the effects of *Andrographis paniculata* methanolic extract as rodenticide on male rats (Dayang & Mahanem 2015). The administration of *Andrographis paniculata* at doses of 800 mg/kg and 1600 mg/kg caused degeneration in

Table 2: Antifertility agents extracted from plants for female

Botanical/Common name	Type of extraction	Part used	Action	References
Artemisia vulgaris Linn (Nagadouna) Family: Asteraceae	Methanol extract	Leaf	Anti-implantation Anti-estrogenic	Kumar et al. 2012; Shaik et al. 2014
Acalypha indica (Kuppi, Kuppikhokhali) Family: Euphorbiaceae	Petroleum ether, Ethanol extract	Whole plant	Anti-implantation Anti-estrogenic	Hirematha et al. 1999
Abroma augusta Family: Malvaceae	Petroleum ether extract	Root	Anti-implantation	Maurya et al. 2004; Raj et al. 2011
Asparagus pubescens Family: Asparagaceae	Methanol extract	Root	Anti-implantation	Nwafor et al. 1998
Beaumontia grandiflora Family: Apocyanaceae	Ethanol extract	Leaf	Anti-implantation Abortifacient	Choudhary et al. 1990
Cayratia trifolia Linn. Family: Vitaceae	Petroleum ether extract	Leaf	Anti-implantation	Gupta et al. 2012
Cuscuta reflexa (Chinailat) Family: Convolvulaceae	Ethanol extract	Whole plant	Anti-implantation	Maurya et al. 2004
Citrullus colocynthis (Tumba, Bitter Apple) Family: Cucurbitaceae	Hydro alcoholic extract	Root, fruit	Anti-implantation	Dehghani et al. 2008
Dictamnus albus Family: Rutaceae	Methanol extract, Hexane extract	Root, bark	Anti-implantation	Mohamed et al. 2014; Woo et al. 1987
Datura metel (Apple of Peru) Family: Solanaceae	Acetone extract	Seed	Anti-implantation	Pandiarajan et al. 2012
Moringa oleifera Family: Moringaceae	Aqueous extract	Root	Anti-implantation	Shukla et al. 1988
Nigella sativa Family: Ranunculaceae	Hexane extract	Seed	Anti-implantation	Keshri et al. 1995

Sertoli cells and germinal cells in the seminiferous tubules and shrinkage of Leydig cells. The results also showed significant decrease in sperm count, serum testosterone level, the weight of testis, number of mountings, and number of fetuses. This is supported by another study (Khaidatul & Mahanem 2017) which examined the reversible spermatotoxic effect of *Andrographis paniculata* on Sprague-Dawley rats. It also showed significant

decrease in sperm count, motility, and viability. Besides, histological analysis of the testicular cells showed the Leydig cell were regressed, the Sertoli cells were damaged, and the lumen of seminiferous tubule was less packed with sperm cells. The administration of this plant extract for 24 days also showed anti-implantation activity in the experimental rats, in which the number of implantation sites decreased with high percentage of infertile male

Table 3: Antifertility agents extracted from plants for male and female

Botanical/Common name	Type of extraction	Part used	Action	References
Aloe barbadensis (Ghretokumari, Aloe Vera) Family: Aloaceae Liliaceae	Aqueous extract, Ethanol extract	Whole plant	Antispermato-genic, Anti-implantation, Spermicidal activity	Kumar et al. 2012; Singh & Gupta 2016; Maurya et al. 2004; Fahim & Wang 1996; Dixit & Joshi 1983; Oyewopo et al. 2011
Andrographis paniculata (Mahatita, Nilavembu, Hempedu bumi, Sambiloto, Family: Acanthaceae	Methanol extract, Alcohol extract	Leaf	Antispermato-genic, Reduces FSH, LH, progesterone and estrogen level	Mohamed et al. 2014; Dayang & Mahanem 2015; Khaidatul & Mahanem 2017; Sakilah et al. 2009
Azadirachta indica (Neem, Dadarek, Veempu) Family: Meliaceae	Ethanol extract, Hexane extract	Leaf, seed, stem/bark	Antispermato-genic, Abortifacient, Spermicidal activity	Kumar et al. 2012; Das et al. 2014; Bhasin et al. 2001; Kabeh & Jalingo 2007
Abrus precatorius Linn (Ghungchi, Rosary Pea) Family: Fabaceae	Methanol extract, Alcohol extract	Seed	Antispermato-genic, Anti-implantation	Kumar et al. 2012; Das et al. 2014; Joshi et al. 2011; Bhatt et al. 2007
Aegle marmelos (Golden Apple, Stone Apple, Shreephal) Family: Rutaceae	Methanol extract, Ethanol extract, Aqueous extract	Leaf, bark	Antispermato-genic, Anti-implantation	Mohamed et al. 2014; Chauhan et al. 2008; Remya et al. 2009
Aristolochia indica (Aaduthinapalai) Family: Aristolochiaceae	Ethanol extract	Root	Antispermato-genic, Anti-implantation	Mohamed et al. 2014; Che et al. 1984
Cuminum cyminum (Jeera) Family: Apiaceae	Ethanol extract	Seed	Anti-implantation, Abortifacient, Antispermato-genic	Venkatesh et al. 2002; Choudhury & Haq 1980; Garg 1976; Nadkarni & Nadkarni 1954
Citrus aurantifolia (Lime) Family: Rutaceae	Juice extract	Fruit	Irregularity of estrous cycle, testicular toxicity	Salawu et al. 2010; Aprioku & Obinime 2014
Centella asiatica (Pegaga) Family: Apiaceae	Ethanol extract	Leaf	Antispermato-genic, Anti-implantation	Mohamed et al. 2014; Yunianto et al. 2010; Yunianto et al. 2017
Curcuma longa Linn (Turmeric, Haldi) Family: Zingiberaceae	Methanol extract, Aqueous extract, Ethanol extract	Rhizome	Antispermato-genic, Anti-implantation	Kumar et al. 2012; Joshi et al. 2011; Purohit 1991
Embelia ribes (False black pepper) Family: Myrsinaceae	Benzene extract	Seed, fruit	Antispermato-genic, Anti-implantation	Mohamed et al. 2014
Hibiscus rosa-sinesis (China rose, Ghudal, Joba) Family: Malvaceae	Methanol extract	Flower, bark	Antispermato-genic	Das et al. 2014
Momordica charantia (Karela) Family: Cucurbitaceae	Petroleum ether, Benzene extract, Alcohol extract	Seed	Antispermato-genic, Anti-implantation	Mohamed et al. 2014; Adewale et al. 2014; Adewale et al. 2014; Tumkiratiwong et al. 2014;Boetse et al. 2011; Yama et al. 2011

rats (80%) in the treated group (1600 mg/kg of *Andrographis paniculata*). In 2009, another study (Niranjan et al. 2010) claimed that the administration of *Andrographis paniculata* (1g/kg) for 28, 42, and 56 days resulted in low follicle stimulating hormone (FSH), luteinizing hormone (LH), and progesterone, and estrogen level in female rats.

Azadirachta indica

Azadirachta indica also known as neem, is one of the natural contraceptive agents. It belongs to the Meliaceae family and acts as spermicidal contraceptive. Since years ago, people have been using *Azadirachta indica* (neem) oil for its various properties. This plant has antispermatogenic property and alters the histology of testis. The aqueous leaves extract of *Azadirachta indica* was proven to decrease the percentage of sperm motility and thus researchers claimed that this plant possesses spermicidal property (Khillare & Shrivastava 2003). A number of studies reported that the administration of *Azadirachta indica* could successfully prevent pregnancy provided it is consumed before sexual intercourse. A single intrauterine administration of neem oil has been proven to block pregnancy in which no implantation was observed in the uterus (Upadhyay et al. 1990). Similarly, a study has proven that the administration of neem seed extract could prevent pregnancy at early post-implantation stage (Mukherjee et al. 1999).

Carica papaya

Carica papaya also known as 'paw paw' is one of the natural contraceptive agents being used widely in many countries. This plant belongs to the family Caricaceae which commonly found in the America. This plant showed antispermatogenic and anti-implantation activity. In 2012, a study has been conducted to investigate the antifertility effects of *Carica papaya* successive chloroform extract in male mice (Christine & Mahanem 2012). It showed that the administration of *Carica papaya* for 14 days resulted in the decrease of sperm count, motility and alteration of testicular morphology. The dose of 200 mg/kg/body weight of this plant showed the most effective dose to decrease the sperm quality and spermatogenesis. Besides that, Julaeha et al. (2015) investigated in vitro study of *Carica papaya* seeds on rat sperm and observed increased abnormality of sperm morphology, motility and viability.

Momordica charantia

Momordica charantia has been widely used for diabetic and antifertility studies (Boetse et al. 2011; Yama et al. 2011). The study conducted by Adewale et al. (2014a) on the antifertility properties of *Momordica charantia* leaves extract on female reproductive hormones showed the reduction of estrogen and progesterone level. In addition, the researchers also had investigated the effect of *Momordica charantia* extract on male fertility hormones. The study showed significant reduction in testosterone and FSH level by suppressing the pituitary-testicular

axis in adult male rats (Adewale et al. 2014b). Besides that, Tumkiratiwong et al. (2014) claimed the reproductive toxicity effect of *Momordica charantia* seed extract in male rats with the reduction of testosterone level, diameter of seminiferous tubule, sperm production, sperm motility, viability and spermatid density. The alteration of seminiferous tubule showed multinucleated giant cells, pyknosis nucleus and revealed atrophy.

MODERN TECHNOLOGY CONTRACEPTION

BARRIER METHODS

Barrier methods or barrier contraceptives are among the many ways of preventing pregnancy by blocking the sperm from passing through the uterine cavity. Male barrier contraceptives include condom, spermicide, and vasectomy. These methods induce sterility, blockage of vas deferens and halt the sperm production. Meanwhile, the female barrier contraceptives include sponge, condom, diaphragms, cervical caps, cervical shield, vaginal cap and tubal ligation.

CONDOM

Condom is the most effective barrier and is readily available. According to (Bromwich & Parsons 1990), the word condom is derived from Persian *kondu* which means a seed store, or Latin word *condus*. It may be also named after a physician, Dr Condom,

who recommended Charles II to use condoms made of either oiled linen or intestines of sheep. The production of condoms began in 1850s when the rubber industry started to develop. Since condom is made of natural rubber and a mixture of few chemical substances, few people are allergic to it and this could make them feel discomfort when using it. It is available in variety of shapes, textures, and colours, which covers the penis to prevent semen, vaginal fluid, and blood from passing through between partners. An "allergy-free" condom that is made of polyurethane is also available for those who are allergic to rubber. The condom for female is made up of thin and transparent soft plastic film which fits loosely inside women's vagina. It prevents the sperm from entering the uterine tract and thus prevents fertilization. Condom also offers protection against sexual transmitted diseases (STD). However, condom should not be used more than once. A new condom must be used for repeated sexual intercourse. In addition, broken condom is not safe because it might cause bacterial or virus infection such as HIV/AIDS. Condom is easily disposable and the most hygienic way to dispose it is by wrapping it with a tissue paper before throwing it away (Bromwich & Parsons 1990).

DIAPHRAGM

Diaphragm is an effective form of female barrier contraceptive. It is made of latex rubber, a dome-shaped device, and comes in a size of 2.5 mm. This

device is filled with spermicidal cream and is placed over the cervix within two hours before sexual intercourse and left in place for 6-8 hours after sexual intercourse (Mohamed et al. 2014). Any sperms that pass through the rubber are eliminated by the cream. There are several types of diaphragms that have been widely used such as coiled spring and flat spring. There are also vaginal barriers such as cervical cap, vault cap, and vimule. Vaginal barriers are used by women who are unable to use diaphragm because of weak vaginal muscles, urinary tract infections, or previous vaginal surgery. These caps are placed in the vagina and suction hold the cap on. It should be removed after 24 hours of sexual intercourse to prevent trauma, odour and infections (Bromwich & Parsons 1990; Advocates 2017; Mohd Azhar 2017).

SPERMICIDES

Studies have reported that 10 to 20 women out of every 100, are likely to get pregnant if they only use spermicide. The probability of pregnancy decreases if both spermicide and barriers are used together. Spermicides are available in various forms such as vaginal tablets, cream, jellies, foaming tablets, aerosols form, c-film (spermicide-impregnated film), and sponge. The spermicidal spreads to the area around the cervix and thus kills the spermatozoa as spermicide acts rapidly. However, using spermicide alone may not lower the rates of pregnancy. It is believed that combining it with other methods is

more effective. For instance, jellies and creams can be used with intrauterine device (IUD) and condoms or with diaphragm or cervical caps if the sexual intercourse occurs more than once within six hours. Spermicide also helps in preventing bacteria and virus infections. However, studies have shown that spermicide could not prevent sexually transmitted infections (Bromwich & Parsons 1990).

STERILIZATION

Sterilization or permanent contraception is the most popular birth control. There are a few options to end fertility via surgery such as vasectomy, also known as man's sterilization, and tubal ligation which cuts the fallopian tubes to prevent fertilization of ovum and sperm. Essure is another option for women which are non-surgical. This procedure can be done within 30 minutes using only local anaesthetic. A special instrument called hysteroscope is inserted into the vagina passing through the cervix and uterus reaching the fallopian tube. The insert will cause the body to form tissue barrier within three months which prevent sperm from reaching the egg.

INTRAUTERINE DEVICE (IUD)

Intrauterine device (IUD) is a T-shaped birth control device for women and is considered 99% more effective at preventing pregnancy. The history of IUD has been studied by (Bromwich & Parsons 1990). It is a device that looks like an old fashioned collar-studs and fits into the cervical canal or the cervix.

Table 4: List of hormonal contraceptives

Trade name	Main compositions
Aranelle®	Ethinyl estradiol, Norethindrone
Apri®	Ethinyl Estradiol, Desogestrel
Aviane®	Ethinyl Estradiol, Levonorgestrel
Anovlar 21®	Ethinyl estradiol, Norethindrone acetate
Azurette®	Ethinyl Estradiol, Desogestrel
Binovum®	Ethinyl estradiol, Norethindrone
Beyaz®	Ethinyl Estradiol, Levomefolate, Drospirenone
Balziva®	Ethinyl Estradiol, Norethindrone
Brevicon®	Ethinyl Estradiol, Norethindrone
Camrese Lo®	Ethinyl Estradiol, Levonorgestrel
Cesia®	Ethinyl Estradiol, Desogestrel
Cryselle®	Ethinyl Estradiol, Norgestrel
Cyclessa®	Ethinyl Estradiol, Desogestrel
Desogen®	Ethinyl Estradiol, Desogestrel
Demulen 50®	Ethynodiol diacetate, Ethinyl Estradiol
Estrostep Fe®	Ethinyl Estradiol, Norethindrone
Enpresse®	Ethinyl Estradiol, Levonorgestrel
Femcon Fe®	Ethinyl Estradiol, Norethindrone
Gianvi®	Ethinyl Estradiol, Drospirenone
Junel®	Ethinyl Estradiol, Norethindrone
Jolessa®	Ethinyl Estradiol, Levonorgestrel
Kelnor®	Ethynodiol, Ethinyl Estradiol
Kariva®	Ethinyl Estradiol, Desogestrel
Loestrin 20®	Ethinyl estradiol, Norethindrone
Levlen®	Ethinyl Estradiol, Levonorgestrel
Levora®	Ethinyl Estradiol, Levonorgestrel
Loryna®	Ethinyl Estradiol, Drospirenone
Lutera®	Ethinyl Estradiol, Levonorgestrel
Lybrel®	Ethinyl Estradiol, Levonorgestrel
Microgynon 30®	Ethinyl estradiol, Levonorgestrel
Modicon®	Ethinyl Estradiol, Norethindrone
Mircette®	Ethinyl Estradiol, Desogestrel
Microgestin®	Ethinyl Estradiol, Norethindrone
MonoNessa®	Ethinyl Estradiol, Norgestimate

Trade name	Main compositions
Necon 1/50®	Mestranol, Norethindrone
Norinyl 1+35®	Ethinyl Estradiol, Norethindrone
Nordette®	Ethinyl Estradiol, Levonorgestrel
Nortrel®	Ethinyl Estradiol, Norethindrone
Ortho TriCyclen Lo®	Ethinyl Estradiol, Norgestimate
Ogestrel®	Ethinyl Estradiol, Norgestrel
Ortho-Novum 1/50®	Norethindrone, Mestranol
Ovcon®	Ethinyl Estradiol, Norethindrone
Ocella®	Ethinyl Estradiol, Drospirenone
Previfem®	Ethinyl Estradiol, Norgestimate
Portia®	Ethinyl Estradiol, Levonorgestrel
Quasense®	Ethinyl Estradiol, Levonorgestrel
Reclipsen®	Ethinyl Estradiol, Desogestrel
Solia®	Ethinyl Estradiol, Desogestrel
Seasonique®	Ethinyl Estradiol, Levonorgestrel
Syeda®	Ethinyl Estradiol, Drospirenone
Sprintec®	Ethinyl Estradiol, Norgestimate
TriLegest Fe®	Ethinyl Estradiol, Norethindrone
Trivora®	Ethinyl Estradiol, Levonorgestrel
TriPrevifem®	Ethinyl Estradiol, Norgestimate
TriNorinyl®	Ethinyl Estradiol, Norethindrone
TriNessa®	Ethinyl Estradiol, Norgestimate
Velivet®	Ethinyl Estradiol, Desogestrel
Yasmin®	Ethinyl Estradiol, Drospirenone
Yaz®	Ethinyl Estradiol, Drospirenone
Zeosa Fe®	Ethinyl Estradiol, Norethindrone
Zovia®	Ethinyl Estradiol, Ethynodiol
Zenchant®	Ethinyl Estradiol, Norethindrone
Zarah®	Ethinyl Estradiol, Drospirenone

It was originally used to treat prolapse of the uterus and abdominal bending which were considered a disease at that time. Some historians mentioned that the IUD practices were developed in the Arab countries. Since a pregnant camel cannot carry heavy loads in the desert, they started placing small pebbles in the uterus of the camels to prevent them from conceiving. Meanwhile, Dr Richter from Germany began publishing information about IUD. The device used was made of silkworm gut but this idea did not get good response until 20 years later when Graefenberg introduced a ring of silkworm gut surrounded by German silver, an alloy of copper, zinc, and nickel. Copper and zinc have been proven able to prevent pregnancy. In 1959 and 1960, Dr Ishihawa in Japan and Dr Margulies in United States have developed the use of plastics IUD. Dr Ishihawa's rings were flexible because it could be squeezed to fit into the uterus and Dr Margulies device can be straightened to ease insertion by (Bromwich & Parsons 1990). However, these developed devices showed a few problems. Firstly, the size was big and could not fit women who have not had pregnancy. Secondly, scientist discovered that the success of IUD depends on the surface area in which the larger the device, the better it prevents pregnancy. In 1968, Zipper developed a medicated IUD that has copper bearing devices. Copper plays an important role in preventing pregnancy and it is a small piece of device which easier, more comfortable, and suits the women who have not had pregnancy (Bromwich & Parsons

1990; Mohd Azhar 2017; OPT 2016; WHO 2018).

HORMONAL METHODS

The hormonal-based contraceptive is an alternative option for birth control. It interrupts the production of spermatozoa, prevents ovulation, and reduces the activity of fallopian tube as well as produces high secretion of cervix to prevent fertilization. There are various types of hormonal contraceptives such as combined oral contraceptives (COCs) pills which contain estrogen and progestin, progesterone-only pills (POPs) which contain only progesterone hormone, combined injectable contraceptives (CICs), combined contraceptives patch, implants, rings, and progesterone only injectable. The COCs pill prevents ovulation and alters the lining of endometrium, hence not allowing fertilization to occur. With proper and consistent use, its effectiveness in preventing pregnancy is 99%. The POPs also prevent ovulation and fertilization of sperm and eggs. While COC and POP are taken orally, CIC is administered by intramuscular injection and it is 99% effective in preventing ovulation and pregnancy. Combined contraceptive patch such as Ortho Evra and combined contraceptive vagina ring such as NuvaRing delivers estrogen and progestin directly into the bloodstream through the skin patch or ring. Progesterone only injectable such as Depo Provera is another hormonal-based contraceptive that requires an injection to prevent ovulation. Implant

is also another type of hormonal contraceptive which contains progesterone hormone. It is a small flexible rod that placed under the skin or upper arm and helps in preventing ovulation. Table 4 shows several hormonal-based contraceptives that have been used worldwide (Josephine 1990; AZA 2011; NIH 2017).

EMERGENCY CONTRACEPTION

Emergency contraception (EC) is used after unprotected sexual intercourse to prevent unintended pregnancy especially among adolescence. However, this type of measure could not protect users from STD. The forms of EC include emergency contraception pills (ECPs) or known as morning-after pills and intrauterine device (IUD). ECPs are orally administrated and it reduces the chance of pregnancy up to 60% if taken up to 120 hours after unprotected sexual intercourse. ECPs such as ulipristal acetate pill (Ella), progestin pill (Norlevo), and Yuzpe are combined with hormonal birth control pills. Although taking ECPs are deemed to be easier, it is less effective compared to IUD. This had been reported by a previous study on the failure of levonorgestrel (LNG) was contributed to ectopic pregnancy (Natasha et al. 2012). IUD can reduce the chances of pregnancy by 99% if it is inserted within seven days after unprotected sexual intercourse. It is believed that the copper ions in the IUD could impair fertilization if it is inserted before ovulation and prevent implantation if it is inserted after ovulation (OPT 2016). Therefore, many

believe that IUD is the most effective emergency contraception for ongoing secure birth control.

CONCLUSION

Contraception has contributed to prevention of unintended pregnancy. Besides, it could also prevent HIV, human papillomavirus (HPV), gonorrhea and chlamydia between partners. The medicinal plants and modern contraceptives are highly effective in improving the reproductive health when it used consistently and in the proper way. Additionally, the health services policies and educational programs also plays an important role in contraceptive access that could improve health outcomes for both males and females.

REFERENCES

- Advocates. 2017. Types of contraception. <https://advocatesforyouth.org/issue/contraceptive-access> [20th June 2017].
- AZA Wildlife Contraception Center. 2011. Current List of Available Birth Control Pills. <https://docplayer.net/23900784-Aza-wildlife-contraception-center.html>. [8th August 2017]
- Aprioku, J.S., Obinime, A.W. 2014. Evaluation of the effects of *Citrus aurantiifolia* (Lime) juice in lead-induced hematological and testicular toxicity in rats. *Pharmacologia* 5(1): 36-41.
- Adeyemi, O.O., Oduyemi, O.I., Ayokunle, O. 2014a. Oral administration of leaf extracts of *Momordica charantia* affect reproductive hormones of adult female Wistar rats. *Asian Pac J Trop Biomed* 4(1): 521-4.
- Adeyemi, O.O., Oduyemi, O.I., Ayokunle, O. 2014b. Evaluation of oral administration of aqueous leaf extract of *Momordica charantia* on fertility hormones of adult male wistar rats. *Global Journal of Pharmacology* 8(2):150-3.
- Bromwich, P., Parsons, T. 1990. *Contraception the facts*. 2nd edition. Oxford: Oxford University Press.
- Bhatt, N., Chawla, S.L., Rao, M.V. 2007. Contraception evaluation of seed extracts of *Abrus precatorius*

- L. in male albino rats (*Mus musculus*). *J Herb Med Toxicol* 1: 45-8.
- Bhasin, S., Woodhouse, L., Casaburi, R., Singh, A.B., Bhasin, D., Berman, N., Chen, X., Yarasheski, K.E., Magliano, L., Dzekov, C., Dzekov, J., Bross, R., Phillips, J., Sinha-Hikim, I., Shen, R., Storer, T.W. 2001. Testosterone dose-response relationships in healthy young men. *Am J Physiol Endocrinol Metab* 281(6): 1172-81.
- Boetse, Y.O., Ikechukwu, D.F., Olugbenga, O.A., Ayodele, O.A., Caramel, N.C. 2011. Histomorphological alterations in the prostate gland and epithelium of seminiferous tubule of Sprague-Dawley rats treated with methanolic extract of *Momordica charantia* seeds. *Iran J Med Sci* 36(4): 266-72.
- Choudhury, R.R., Haq, M. 1980. Review of plants screened for antifertility activity. *J Bullt Med Ethno Bot Res* 1: 408-18.
- Choudhary, D.N., Singh, J.N., Verma, S.K., Singh, B.P. 1990. Antifertility effects of leaf extracts of some plants in male rats. *Indian J Exp Biology* 28: 714-6.
- Che, C.T., Ahmed, M.S., Kang, S.S., Waller, D.P., Bingle, A.S., Martin, A, Rajamahendran, P., Bunyapraphatsara, N., Lankin, D.C. Cordell, G.A. 1984. Studies on aristolochia III. Isolation and biological evaluation of constituents of *Aristolochia indica* roots for fertility-regulating activity. *J Nat Prod* 47(2): 331-41.
- Chauhan, A., Agarwal, M., Kushwaha, S., Mutreja, A. 2008. Antifertility studies of *Aegle marmelos* (Corr.) an Indian medicinal plant on male albino rats. *Egypt J Biol* 10: 28-35.
- Christine, C.C., Mahanem, M.N. 2012. Antifertility and reversible effect of extract successive chloroform of papaya seeds (*Carica papaya*) on fertility of male mice. Thesis. Universiti Kebangsaan Malaysia.
- Dayang, N.F., Mahanem, M.N. 2015. Fertility suppression in male sprague-dawley rats by administration of methanolic extract of Hemptedu Bumi (*Andrographis paniculata*). *Sains Malaysiana* 44(9): 1249-55.
- Das, B., Talukdar, A.D., Choudhury, M.D. 2014. A few traditional medicinal plants used as antifertility agents by ethnic people of Tripura, India. *Int J Pharm Pharm Sci* 6(3): 47-53.
- Dixit, V.P., Joshi, S. 1983. Effect of *Aloe barbadensis* and *Clofibrate* in triton induced hyperlipidaemic presbytis monkey. *Ind J Med Res* 78: 417-21.
- Dehghani, F., Azizi, M., Panjehshahin, M.R., Talei-Khozani, T., Mesbah, F. 2008. Toxic effects of hydroalcoholic extract of *Citrullus colocynthis* on pregnant mice. *Iranian J Vet Res* 9(1): 42-5.
- Fahim, M.S., Wang, M. 1996. Zinc acetate and lyophilized *Aloe barbadensis* as vaginal contraceptive. *J Contraception* 53(4): 231-6.
- Gupta, R.S., Kumar, P., Dixit, V.P., Dobhal, M.P. 2000. Antifertility studies of the root extract of *Barleria prionitis* in male albino rats with special reference to testicular cell population dynamics Linn. *J Ethnopharmacology* 70(2): 111-17.
- Gupta, R.S., Kachhawa, J.B., Chaudhary, R. 2004. Antifertility effects of methanolic pod extract of *Albizia lebbbeck* (L.) Benth in male rats. *Asian J Androl* 6: 155-9.
- Gupta, R.S., Chaudhary, R., Yadav, R.K., Verma, S.K., Dobhal, M.P. 2005. Effect of saponins of *Albizia lebbbeck* (L.) Benth bark on the reproductive system of male albino rats. *J Ethnopharmacology* 96(1-2): 31-6.
- Gupta, R.S., Kacchawa, J.B. 2007. Evaluation of contraceptive activity of methanol extract of *Dendrophthoe falcata* stem in male albino rats. *J Ethnopharmacology* 112(1): 215-8.
- Gupta, A., Bhardwaj, A., Gupta, J., Bagchi, A. 2012. Antiimplantation activity of petroleum ether extract of leaves of *Cayratia trifolia* Linn. on female Albino rat. *Asian Pac J Trop Biomed* 2(1): 197-9.
- Ghosh, A., Jana, K., Pakhira, B.P., Tripathy, A., Ghosh, D. 2015. Anti-fertility effect of aqueous-ethanolic (1:1) extract of the fruit of *Terminalia chebula*: Rising approach towards herbal contraception. *Asian Pac J Reprod* 4(3): 201-7.
- Garg, S.K. 1976. Antifertility screening of plants. Effect of four indigenous plants on early pregnancy in female albino rats. *Ind J Med Res* 50: 435-8.
- Hirematha, S.P., Rudresh, K., Badami, S., Patil, S.B., Patil, S.R. 1999. Post-coital antifertility activity of *Acalypha indica* L. *J Ethnopharmacology* 67(3): 253-8.
- Josephine, B. 1990. *Lecture notes of gynaecology*. P.G. Publishing Pte. Ltd. Blackwell Scientific Publication.
- Joshi, S.C., Sharma, A., Chaturvedi, M. 2011. Antifertility potential of some medicinal plants in males: an overview. *Int J Pharm Pharm Sci* 3(5): 204-17.
- Julaeha, E., Permatasaria, Y., Mayantia, T., Diantinib, A. 2015. Antifertility compound from the seeds of *Carica papaya*. *Procedia Chemistry* 17: 66-9.
- Kabeh, J.D., Jalingo, M. 2007. Exploiting neem (*Azadirachta Indica*) resources for improving the quality of life in Taraba State, Nigeria. *Int J Agri Biol* 9(3): 530-2.
- Kamal, R., Gupta, R.S., Lohiya, N.K. 2003. Plants for male fertility regulation. *Phytother Res* 17(6): 579-90.
- Keshri, G., Singh, M.M., Lakhmi, V., Kamboj, V.P. 1995. Post-coital contraceptive efficacy of the seeds of *Nigella sativa* in rats. *Indian J Physiol Phannacol* 39(1): 59-62.
- Khaidatul, A.K., Mahanem, M.N. 2017. Reversible spermatotoxic effect of *Andrographis paniculata* methanol extract in sprague dawley rats. *Malays Appl Biol* 46(1): 225-32.

- Khillare, B., Shrivastava, T.G. 2003. Spermicidal activity of *Azadirachta indica* (neem) leaf extract. *Contraception* **68**(3): 225-9.
- Khillare, B., Singh, A.R. 2014. Spermicidal activity of *Elettaria cardamomum* and *Cuminum cyminum* seed extracts and assessment of sperm function in albino rats. *Int J Pharmacogno* **1**(4): 258-65.
- Kutney, J.P., Hewitt, G.M., Lee, G., Piotrowska, K., Roberts, M., Rettig, S.J. 1992. Studies with tissue cultures of the Chinese herbal plant, *Tripterygium wilfordii*. Isolation of metabolites of interest in rheumatoid arthritis, immunosuppression, and male contraceptive activity. *Can J Chem* **70**(5): 1455-80.
- Kumar, D., Kumar, Prakash, O. 2012. Potential antifertility agents from plants: a comprehensive review. *J Ethnopharmacol* **140**(1): 1-32.
- Lohiya, N.K., Goyal, R.B. 1992. Antifertility investigations on the crude chloroform extract of *Carica papaya* Linn. seeds in male albino rats. *Indian J Exp Biol* **30**(11): 1051-5.
- Maurya, R., Srivastava, S., Kulshreshta, D. Gupta, C.M. 2004. Traditional remedies for fertility regulation. *Curr Med Chem* **11**(11): 1431-50.
- Mohamed, G.A., Ibrahim, S.R.M., Al Haidari, R.A. 2014. A review on natural contraceptive agents. *Am J Pharm Tech Res* **4**(3): 124-57.
- Mohd Azhar, M.N. 2017. Simplified gynaecology for medical students. UPNM: Universiti Pertahanan Nasional Malaysia Press.
- Mukherjee, S., Garg, S., Talwar, G.P. 1999. Early post implantation contraceptive effects of a purified fraction of neem (*Azadirachta indica*) seeds, given orally in rats: possible mechanisms involved. *J Ethnopharmacology* **67**(3): 287-96.
- Nadkarni, A.K., Nadkarni, K. 1954. *Indian Materia Medica* 3rd edition. Bombay, Popular Book Depot.
- Natasha, M.N., Khoo, H.W., Sulaiman, A.S., Nur Azurah, A.G., Md Dali, A.Z.H., Jamil, M.A. 2012. Ectopic pregnancy following Levonorgestrel-only emergency contraception: The First Malaysian Case Report. *Med & Health* **7**(2): 107-11.
- Niranjan, A., Srisuwan, S., Tewari, S.K., Lehri, A. 2010. Biological activities of kalmegh (*Andrographis paniculata* Nees) and its active principles-A review. *Indian J Nat Prod Resour* **1**: 125-35.
- Nurlaily, A., Noor Baitee, A.R., Musalmah, M. 2012. Comparative antioxidant and anti-inflammatory activity of different extracts of *Centella asiatica* (L.) urban and its active compounds, asiaticoside and madecassoside. *Med & Health* **7**(2): 62-72.
- Nwafor, P.A., Okwuasaba, F.K., Onoruvweb, O.O. 1998. Contraceptive and non-estrogenic effects of methanolic extract of *Asparagus pubescens* root in experimental animals. *J Ethnopharmacol* **62**(2): 117-22.
- Options for Sexual Health. 2016. Intrauterine devices. <https://www.optionsforsexualhealth.org/> [8th August 2017].
- Options for Sexual Health. 2016. Sexual and Reproductive Health Care and Education <https://www.optionsforsexualhealth.org/>. [8th August 2017]
- Oyewopo, A.O., Oremosu, A.A., Akang, E.N., Noronha, C.C., Okanlawon, A.O. 2011. Effects of Aloe Vera (*Aloe Barbadosis*) aqueous leaf extract on testicular weight, sperm count and motility of adult male sprague-dawley rats. *J American Science* **7**(4): 31-4.
- Pandiarajan, G., Govindaraj, R., Makesh, K.B., Sankarasivaraman, K. 2012. Antifertility activity in the acetone extracts of *Datura metel*, L seeds on female mouse. *J Pharmacogenomics Pharmacoproteomics* **3**(4): 111.
- Pant, N., Srivastava, S.C., Prasad, A.K., Shankar, R., Srivastava, S.P. 1995. Effects of carbaryl on the rat's male reproductive system. *Vet Hum Toxicol* **37**(5): 421-5.
- Pant, N., Murthy, R.C., Srivastava, S.P. 2004. Male reproductive toxicity of sodium arsenite in mice. *Hum Exp Toxicol* **23**(8): 399-403.
- Pei Gen, X., Nai Gong, W. 1991. Can ethnopharmacology contribute to the development of antifertility drugs. *J Ethnopharmacol* **32**(1-3): 167-77.
- Purohit, A. 1991. Contraceptive efficacy of *Curcuma longa* (50% EtOH extract) with special emphasis on testicular population dynamics. *J Curr Biosci* **8**(4): 129-34.
- Qian, S.Z. 1987. *Tripterygium wilfordii* chinese herb effective in male fertility regulation. *J Contraception* **36**(3): 335-45.
- Raj, A., Singh, A., Sharma, A., Singh, N., Kumar, P., Bhatia, V. 2011. Antifertility activity of medicinal plants on reproductive system of female rat. *Int J Bio-Eng Sci Technol* **2**(3): 44-50.
- Remya, M., Sharma, R.C., Deepali, M., Sakshi, B., Nilesh, P., Tharini, S. 2009. In vitro effects of *Aegle marmelos* on human sperm. *Vitality Biomedicine* **29**(2): 183-5.
- Shaik, A., Kanhere, R., Cuddapah, R., Nelson, K., Vara, P., Sibyala, S. 2014. Antifertility activity of *Artemisia vulgaris* leaves on female Wistar rats. *Chin J Nat Med* **12**: 180-5.
- Sakilah, S., Begum, N., Kawsar, S. Begum, Z.A., Zoha, M.S. 2009. Relationship of anti-fertility effects of *Andrographis paniculata* and hormonal assay in female rats. *Bangladesh Journal of Medical Science* **8**(1-2): 10-4.
- Salawu, A.A., Osinubi, A.A., Dosumu, O.O., Kusemiju, T.O., Noronha, C.C., Okanlawon, A.O. 2010. Effect of the juice of lime (*Citrus Aurantifolia*) on estrous cycle and ovulation of Sprague dawley rats. *Endocr Pract* **16**(4): 561-5.
- Sailani, M.R., Moeini, H. 2007. Effect of *Ruta graveolens* and *Cannabis sativa* alcoholic

- extract on spermatogenesis in the adult Wistar male rats. *Indian J Urol* 23: 257-60.
- Singh, K., Gupta, R.S. 2016. Antifertility activity of β -sitosterol isolated from *Barleria Prionitis* (L.) Roots in male albino rats. *Int J Pharm Pharm Sci* 8(5): 88-96.
- Shukla, S., Mathur, R., Prakash, A.O. 1988. Antifertility profile of the aqueous extract of *Moringa oleifera* roots. *J Ethnopharmacol* 22(1): 51-62.
- Srivastava, S., Singh, G.B., Srivastava, S.P., Seth, P.K. 1990. Testicular toxicity of di-n-butyl phthalate in adult rats: effect on marker enzymes of spermatogenesis. *Indian J Exp Biol* 28(1): 67-70.
- Tumkiratiwong, P., Ployattarapinyo, R., Pongchairerk, U., Thong-Asa, W. 2014. Reproductive toxicity of *Momordica charantia* ethanol seed extracts in male rats. *Iran J Reprod Med* 12(10): 695-704.
- Udoh, P., Kehinde, A. 1999. Studies on antifertility effect of pawpaw seeds (*Carica papaya*) on the gonads of male albino rats. *Phytother Res* 13(3): 226-8.
- Udoh, P., Essien, I., Udoh, F. 2005. Effects of *Carica papaya* (paw paw) seeds extract on the morphology of pituitary-gonadal axis of male Wistar rats. *Phytother Res* 19(12): 1065-8.
- Upadhyay, S.N., Kaushic, C., Talwar, G.P. 1990. Antifertility effects of neem (*Azadirachta indica*) oil by single intrauterine administration: a novel method for contraception. *Proc Biol Sci* 242(1305): 175-9.
- U.S. National Library of Medicine. 2017. Estrogen and Progestin (Oral Contraceptives). <https://medlineplus.gov/druginfo/meds/a601050.html>. [21st June 2017].
- Verma, P.K., Sharma, A., Joshi, S.C., Gupta, R.S., Dixit, V.P. 2005. Effect of isolated fractions of *Barleria prionitis* root methanolic extract on reproductive function of male rats: preliminary study. *Fitoterapia* 76: 428-32.
- Venkatesh, V., Sharma, J.D., Kamal, R. 2002. A comparative study of effect of alcoholic extracts of *Sapindus emarginatus*, *Terminalia bellerica*, *Cuminum cyminum* and *Allium cepa* on reproductive organs of male albino Rats. *Asian J Exp Sci* 16(1-2): 51-63.
- Woo, W.S., Lee, E.B., Kang, S.S., Shin, K.H., Chi, H.J. 1987. Antifertility principle of *Dictamnus albus* root bark. *Planta Medica* 53(5): 399-401.
- World Health Organization. 2018. Family planning/Contraception. <http://www.who.int/news-room/fact-sheets/detail/family-planning-contraception> [28th June 2018].
- Yama, O.E., Osinubi, A.A., Duru, F.I.O., Noronha, C.C., Okanlawon, A.O. 2011. Contraceptive effect of methanolic extract of *Momordica charantia* seed in male Sprague-Dawley rats. *Asian J Pharm Clin Res* 4(2): 22-6.
- Yunianto, I., Das, S., Mahanem, M.N. 2010. Antispermatic and antifertility effect of pegaga (*Centella asiatica* L.) on testis of Sprague Dawley rats. *La Clinica Terapeutica* 161(3): 235-9.
- Yunianto, I., Bashah, N.A., Noor, M.M. 2017. Antifertility properties of *Centella asiatica* ethanolic extract as a contraceptive agent: Preliminary study of sperm proteomic. *Asian Pac J Reprod* 6: 212-6.

Received: 6 June 2018

Accepted: 13 Aug 2018