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Journal of Ethnopharmacology





Review Medicinal plants used for contraception in South Africa: A review

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ARTICLE INFO	A B S T R A C T
Keywords: Child spacing Contraceptive Hormonal contraceptives Indigenous medicinal plants Traditional medicine	 Ethnopharmacological relevance: The indigenous people of South Africa, such as the Khoisan, Zulu, and Ndebele, have used medicinal plants for contraception. One of the reasons for using contraception among indigenous communities is for child spacing. Aim of the study: The study aims to review medicinal plants used for contraception in South Africa as potential sources for the discovery and development of safe male and female hormonal contraceptives. Materials and methods: A literature search was conducted on medicinal plants used for contraception in South Africa by referencing textbooks and scientific databases such as Google Scholar, Science Direct, PubMed, North-West University Institutional Repository, National ETD Portal, government policies and documents on contraception, these and dissertations, and other web sources such as records from SANBI and PROTA. Results: A minimum of 25 medicinal plants were identified as being used for contraception in South Africa, and these plants included local and exotic plants. Medicinal plants with contraceptive activity are Bulbine latifolia, Pouzolzia mixta, Salsola tuberculatiformis, Securidaca longipedunculata, and Typha capensis. In vivo and in vitro studies showed a decrease in mount, intromission and ejaculatory frequencies, inhibition of implantation, contraceptive effect, displaced glucocorticoids, and prolonged diestrus or had negative effects on vitality, motility, and sperm production. Conclusions: Some of the plants used for contraception in South Africa are toxic to both animals and humans. Research is needed focusing on medicinal plants used by men for contraception policies and interventions. Medicinal plants such as B. latifolia and P. mixta demonstrated that medicinal plants used for contraception policies and interventions. Medicinal plants sucres for the discovery and development of safe male and female hormonal contraceptives.

1. Introduction

The initiation of pregnancy comprises two processes: fertilization and implantation (Theron and Grobler, 1998). Contraception, on the one hand, refers to the prevention of conception (fertilization), but generally, it means the prevention of pregnancy (Pathak et al., 2005). The target of contraceptive means is to prevent the release of sperms in the reproductive tract of the male (ejaculation), release of egg from the ovary (ovulation), union of egg and sperm in the oviduct (fertilization), and attachment of embryo to the uterus wall (implantation). On the other hand, abortion refers to termination of the developing embryo from the uterus (Anand et al., 2015). Roux (1995) defined abortion as "the expulsion of a living fetus with the express purpose of killing it." The use of medicinal plants for family planning has been grouped into different categories, namely, spermicides, contraceptives, and abortifacients, to clearly define their role viz-a-viz the type of family planning (Alade et al., 2018). Plants regarded as spermicides can destroy viable sperms. Medicinal plants regarded as contraceptives are those capable of preventing pregnancy by interfering with the normal process of ovulation, fertilization, and implantation of a fertilized egg, whereas plants regarded as abortifacients are those that disturb the embryo that is already implanted in the uterine lining and cause premature termination of pregnancy (Namulindwa et al., 2015). Globally, medicinal plants have been used as contraceptive agents in different countries (Keshri et al., 2003).

Interventions (e.g. herbal decoctions) to avoid pregnancy after

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https://doi.org/10.1016/j.jep.2019.02.002

Received 3 July 2018; Received in revised form 1 February 2019; Accepted 1 February 2019 Available online 04 February 2019 0378-8741/ © 2019 Elsevier B.V. All rights reserved.

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sexual intercourse already existed among women in precolonial Sub-Saharan Africa (Agadjanian, 1999). Medicinal plants are used as contraceptives in Tanzania (Keele et al., 2005), Uganda (Ntozi and Kabera, 1991; Kabagenyi et al., 2016), Zimbabwe (Jaravaza, 2013), and South Africa (Mothiba et al., 2012). It is presently generally accepted that current modern fertility control methods are inadequate to meet the varied and changing personal needs of couples at different times in their reproductive lives and in the widely differing geographical, cultural, and religious settings that exist worldwide (Sathiyaraj et al., 2012).

Globally, there is an urgent need to replace harmful and unreliable modern contraceptives with safe and effective indigenous contraceptives, especially those derived from medicinal plants (Kumar et al., 2012). The current contraceptive options for men are not ideal (Cheng and Mruk, 2010). There are concerns that vasectomy is irreversible (Glasier, 2010). The failure rate of condoms is unacceptably high (Cheng and Mruk, 2010), while early withdrawal is unreliable and always problematic (O' Rand et al., 2015). As a result, it is important to identify a hormonal male contraceptive that is effective, reversible, and safe (Wang et al., 2016).

On the other hand, National Contraception and Fertility Planning Policy and Service Delivery Guidelines (2012) list access to contraceptive service as one of the factors influencing contraceptive use in South Africa (Department of Health, Republic of South Africa, 2012). The location of a health facility and the operational hours are two of the most important factors preventing pregnant women from using family planning services (Molebatsi et al., 2013). Furthermore, there is a belief that modern contraceptives have side effects such as hormonal imbalance, hypertension, increased risk of cancer, weight gain, nausea, headache, depression, cardiovascular disease, abdominal pain, heavy menstrual bleeding, and genital infections (Oddens, 1999).

Medicinal plants are the most easily accessible health resource available to many rural communities (Dar et al., 2017) and poses low toxicity (Pradhan et al., 2012). The safety of many of the herbal drugs used as contraceptives is only relative, but the population feels more assured because of their long and widespread usage and their familiarity with these plants (Ogbuewe et al., 2011). Where poisoning from medicinal plants has been reported, it usually has been due to misidentification of the plants in the form in which they are sold or due to incorrect preparation and administration by inadequately trained personnel (Nasri and Shirzad, 2013a, 2013b). Anecdotal data emphasize the safety of medicinal plants used as contraceptives. Herbal contraceptives may offer alternate ways for women who lack access to modern contraception such as postcoital contraceptives. Herbal contraceptives may also be of assistance to women who experience health problems due to side effects associated with modern contraception (Anand et al., 2015).

The capacity for vertebrates to reproduce is dependent on a functional hypothalamic–pituitary–gonadal (HPG) axis (Maffucci and Gore, 2009). The HPG axis is a hormone system whereby the hypothalamus secretes gonadotropin-releasing hormone (GnRH), which is transported through the blood to the pituitary gland. In this gland, the GnRH induces the production and secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which are, in turn, transported by the blood to the ovaries and testes (Kong et al., 2014). A schematic representation of male and female HPG axes is shown in Figs. 1 and 2, respectively.

The mechanisms of action of hormonal male contraception are based on the suppression of the secretion and production of the gonadotropins, both LH and FSH, from the pituitary gland by exogenous sex steroids (androgens with or without progestins) or GnRH analogs.

Gonadotropin suppression results in a marked decrease in intratesticular testosterone and suppression of spermatogenesis (Wang et al., 2016). Medicinal plant extracts exhibiting reduced levels of testosterone, LH, and FSH are thus potential agents in developing male contraceptives (Abdillahi and Van Staden, 2012).

The site of action of antifertility agents in females consists of the





Fig. 1. Schematic representation of the male hypothalamic–pituitary–gonadal (HPG) axis. (Adopted from Kong et al., 2014).





Fig. 2. Schematic representation of the female hypothalamic–pituitary–gonadal (HPG) axis. (Adopted from Kong et al., 2014).

hypothalamus, anterior pituitary, ovary, oviduct, uterus, and vagina. The hypothalamus controls the action of the uterus through FSH and LH (Pradhan et al., 2012). LH and FSH travel through the bloodstream and act on receptors in ovaries, thereby stimulating gametogenesis and the secretion of estrogen and progesterone (MacManes et al., 2017). Estrogen and progesterone prevent the secretion of FSH and LH from the anterior pituitary, and this indirectly affects the maturation of Graafian follicles and the release of the egg through a negative feedback effect. Plants with an estrogenic property can directly influence pituitary action by peripheral modulation of LH and FSH, which decreases the secretion of these hormones. The decrease in LH and FSH could explain ovulation and estrous cycle blockage by some plant extracts (Pradhan et al., 2012).

Medicinal plants used for contraception that show contraceptive activity by influencing reproductive hormones without any signs of toxicity such as mortality and morbidity are potential sources for the

Table 1 Medicinal plants used for cont	traception in South	n Africa. Family and s	pecies were validated taxonomic	ally using The Plar	it List (http://ww	w.theplantlist.org	О.	
Species	Family	Common names	^a Vernacular name(s)	^b Provincial distribution	Conservation status	Part used/ Investigated	Preparation/Administration	References
Acalypha brachiata Krauss	Euphorbiaceae	Heart-leaved brooms and brushes	Umpendulu (Z), "Makgonatsothe" and "Mogaloriodumela" (T), Uvelabahleka (Z)	L, M, NW, KZN, GP, EC.	Not listed	Roots	A root decoction is drunk.	Watt and Breyer- Brandwijk (1962)
Aloe spp. (species unspecified)	Xanthorrhoeaceae	Bitter aloe, Tap aloe, Red aloe	Lekgala (T), iNhlaba (Z), iKhala (X)	EC, FS, KZN, WC.	Not listed	Leaves	Leaf sap is taken orally by women.	Hutchings et al. (1996)
Bulbine latifolia (L.f.) Spreng.	Xanthorrhoeaceae	Snake flower, cats' tail, bum jelly plant, grass aloe.	Rumo la madi (T), Ibhucu (Z), Sehlare-sa-mollo (S), Intelezi, ingelwane (X),	EC, KZN, FS, M, L, NW.	Not listed	Stem	Unspecified.	Yakubu and Afolayan (2009a)
Centaurea benedicta (L.) L.	Compositae	Holy thistle	Karmedik (A)	WC.	Not listed	Whole plant	Infusion of the whole plant is taken.	Deutschländer et al. (2009)
Cordia monoica Roxb.	Boraginaceae	Sandpaper, Saucer- berry.	Isidakwa, Ilovu-elimyama, ilovu- lasemfuleni (Z).	KZN, L, M.	Least concern	Roots	Unspecified	Cambie and Brewis
Dioscorea dregeana (Kunth) T. Durand & Schinz	Dioscoreaceae	African Wild yam	Ingcolo (X),	L, M, KZN, EC.	Least concern	Unspecified	Unspecified	Wink and Van Wyk (2008)
Englerophytum magalismontanum (Sond.) T. D. Penn.	Sapotaceae	Transvaal milkplum	Motlhatswa (T), Munombelo (V), Amanumbelo (Z)	GP, NW, M, L, KZN.	Least concern	Unspecified	Unspecified	Mabogo (1990)
<i>Flueggea virosa</i> (Robx.exWilld.) Rovle	Phyllanthaceae	White berry-bush	Muhlakaume (S)	L, P, M, KZN.	Not listed	Roots	Eaten before sexual intercourse.	Tabuti (2007)
Garcinia livingstonei T. Anderson	Clusiaceae	Livingstone's garcinia, African mangosteen	Muphiphi (V), Umgobandlovu, UmPhimbi (Z), Mmimbi (T), Mokonstono (S)	KZN, L. M.	Least concern	Roots	Unspecified	Mabogo (1990)
Gymnanthemum myrianthum (Hook.F.) H. Rob.	Compositae	Blue bitter-tea, poison tree	Mululudza (V), uHluhlunga (Z)	KZN, L, M.	Least concern	Roots	An infusion of soaked or boiled root is drunk two or three times a day	Mabogo (1990)
Kedrostis nana Cogn. Dicerothamnus rhinocerotis (L.f.) Koek.	Cucurbitaceae Compositae	Bitter karkoe Rhinoceros bush, rhenoster bush	Bitter patat (A) renosterbos, rhenosterbos (Afr.)	WC, KZN. EC, NC.	Least concern Least concern	Tuber Leafy stems	A decoction of cooked and baked tuber of <i>Kedrostis nana</i> is mixed with boiled leafy stems of <i>Dicerothamus</i>	Rood (1994)
<i>Leucaena leucocephala (</i> Lam.) de Wit	Leguminosae	White lead tree	Ubobo, Ulusina (Z)	KZN, GP, M, NW.	Not Listed	Bark, leaves, seeds	nunoea ous and taken otany Unspecified	Dzoyem and Eloff (2015)
Mucuna coriacea Baker	Leguminosae	Hell-fire bean, Fire bean, Buffalo-bean,	Vhaulada (V), Mulada (V)	GP, L, M.	Least concern	Roots	Roots are boiled, and the mixture is taken orally.	Mahwasane et al. (2013)
Olea europaea L.	Oleaceae	Wild olive	Mothhware (T), Motholoari (S), Umquma (X)	WC, EC, FS, KZN, M, L, GP, NW,	Least concern	Unspecified	Unspecified	Abdillahi and Van Staden (2012) ^c
Olea exasperate Jacq.	Oleaceae	Dune olive		EC, WC.	Not listed	Unspecified	Unspecified	Abdillahi and Van Staden (2012) ^c
Kigelia africana (Lam.) Benth.	Bignoniaceae	Sausage tree	Worsboom (A), umVunguta, umFongothi (Z), Muvevha (V)	KZN.	Least concern	Bark	The root of Acalypha brachiata and the bark of Kigelia africana are boiled and half a cup of it is taken three times a day	de Wet and Ngubane (2014)
Polygonum aviculare L.	Polygalaceae	Knotweed	Koperdraad (A) Lirahadibonoe (S)	Unspecified	Not listed	Unspecified	Unspecified	Hulley and Van Wyk (2018)
Pouzolzia mixta Solms	Urticaceae	Soap-nettle, Soap- brush	Udekane (Z), Murovhadembe, (V), Isikhukhukhu (N),	KZN, M GP, NW, L.	Least concern	Roots	A root infusion is taken orally once a day	Van Wyk and Gericke (2000)
Salsola tuberculatiformis Botsch.	Amaranthaceae	Cauliflower, Saltwort	Not found	NC.	Least concern	Unspecified	Aqueous extracts orally taken by women.	Maritz (1969)
Schkuhria pinnata (Lam.) Kiintze ex Thell.	Compositae	Dwarf Mexican marioold	Ruhwahwa (Z), 1 newielo (V)	NW, L.	Not listed	Whole plant	An infusion of the whole plant is taken shortly hefore intercourse.	Van Wyk and Gericke (2000)
Securidaca longipedunculata Fresen.	Polygalaceae	Violet tree	Mpesu (V), Mmaba (T),	NW, L, GP.	Not listed	Roots	Decoction is taken orally	Mabogo (1990)

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Table 1 (continued)								
Species	Family	Common names	^a Vernacular name(s)	^b Provincial distribution	Conservation status	Part used/ Investigated	Preparation/Administration	References
Trachyandra muricata (L.f.) Kunth	Xanthorrhoeaceae	Olifant foot	Tsila tsila (S)	NC, WC.	Least concern	Rhizome	Unspecified	Philander (2011)
Typha capensis (Rohrb.) N.E.Br.	Typhaceae	Bulrush	Ibhuma (Z), Motsitla (S)	EC, FS, GP, KZN, L, M. NW. NC. WC.	Least concern	Roots	Unspecified	Mabogo (1990)
Withania somnifera (L.) Dunal	Solanaceae	Winter cherry	Bofepha (S), ubuvuma (X), ubuvimbha (Z)	KZN, FS, EC.	Least concern	Leaves, bark, roots	Unspecified	Devi (1996)

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^a Vernacular names (S = Sotho, T = Tswana, X = Xhoza, V = Venda, Z = Zulu, A = Afrikaans).

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Provinces: EC (Eastern Cape, FS (Free State), GP (Gauteng), KZN (KwaZulu-Natal), L (Limpopo), (M) Mpumalanga, (NC) Northern Cape, NW (North West), WC (Western Cape).

Secondary source referenced; primary source could not be found on /http://www.uwc.ac.za

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discovery and development of safe male and female hormonal contraceptives. In vivo, in vitro, and toxicity studies are included in the review in the hope of identifying such plants. The study aims to review medicinal plants used for contraception in South Africa as potential source for the discovery and development of safe male and female hormonal contraceptives.

2. Materials and methods

The review began by conducting a literature search on medicinal plants traditionally used for contraception in South Africa (Table 1) by referencing ethnobotanical textbooks and scientific databases such as Google Scholar: Science Direct: Scopus: EBSCO: North-West University Institutional Repository; National ETD Portal-South African theses and dissertations. Other web records from South African National Biodiversity Institute (SANBI), Plant Resources of tropical Africa (PROTA), thesis, dissertations, and government documents and policies.

The following search terms were used: contraception, contraceptives, prevention of pregnancy, traditional medicines, indigenous contraception, medicinal plants, and herbal contraceptives. The identified medicinal plants included both indigenous and exotic species reported to be used for contraception in South Africa. The search criteria for medicinal plants used for contraception in South Africa included plants that showed contraceptive activity when evaluated in vivo or/and in vitro.

Medicinal plants given in Table 1 that were reported to show contraceptive activity when evaluated in vivo and/or in vitro locally were grouped together in Table 2. Only published articles from research conducted in South Africa were considered for in vivo and/or in vitro studies (Table 2). Finally, information about the toxicity of each medicinal plant listed in Table 2 (plants that showed contraceptive activity) recorded.

The Plant List (www.theplantlist.org) Version 1.1 (September 2013) database was used to validate the scientific names of all species and family identified. The South African National Biodiversity Institute (SANBI) 2017 Red Data List version 2017.1 (http://redlist.sanbi.org/) was used to evaluate the national status and criteria assessment of the identified plants.

3. Results and discussion

In this review, a minimum of 25 medicinal plants were identified as some of the plants used for contraception in South Africa (Table 1). This review makes a distinction between contraception and antifertility, family planning, birth control, and (early) abortion. Medicinal plants referred to in literature as being used for family planning, antifertility, birth control, or (early) abortion were excluded on the basis of the definition of contraception made in this review. The number of medicinal plants used for contraception in South Africa is therefore probably higher than that identified in this review for two reasons: first, because contraception as a concept is sometimes treated as a synonym to antifertility, family planning, birth control, and early abortion, and second, because contraception is embedded within and part of antifertility, family planning, and birth control. Abortion is considered termination and not prevention of pregnancy.

Exotic medicinal plants used specifically for contraception in South Africa or that showed contraceptive activity when evaluated in vivo or in vitro locally were included in the review. Exotic plants were included in the review as an appreciation for the dynamic and evolutionary nature of African traditional medicine (ATM), as well as to increase the scope of potential plant candidates for the discovery and development of safe male and female hormonal contraceptives in South Africa.

3.1. Ethnobotanical knowledge of contraception

National Contraception Clinical Guidelines (2012) recommend that

Table 2 In vivo and in vitro inve	stigations c	conducted loc	ally on some of t	he medicinal plan	ts used for con	traception in South Africa	-i			
Species	Test model	Animal tested	Extract used	Control	Part used	Doses tested	Duration	Administration	Results/mechanisms of action	Reference
Bulbine latifolia (L.f.) Spreng.	In vivo	Male rat	Water	Water	Stem	25, 50, and 100 mg/kg body weight	7 days	Oral	The extract for 100 mg/kg body weight significantly decreased the serum testosterone and progesterone, mount, intromission, and ejaculatory frequencies.	Yakubu and Afolayan (2009a)
Pouzolzia mixta Solms	In vivo	Female Sprague Dawley rat	Water and ethanol	Normal saline	Roots	300 mg/kg body weight	7 days before and 10 days after mating	Oral	Both aqueous and ethanolic <i>P. mixta</i> extracts for 300 mg/kg body weight inhibited implantations	Sewani-Rusike (2013)
Salsola tuberculatiformis Botsch	In vivo	Female Wistar rat	Not specified	Control A (20 g of rat feed treated with 5 ml of 96% ethanol) Control B injected with 0.5 ml PBS only.	unspecified	0.16-94 µmol per day orally and 0.16-3.4 µmol intraperitoneally	16 days	Oral and intraperitoneal	An analog of phenylaziridine precursors (Compound A) had a contraceptive effect on female Wistar rats	Louw et al. (1997)
	In vitro	Rat blood samples	Not specified	No control	Unspecified	0.396 and 6.34 mM	20 s	Not applicable	Compound A significantly displaced glucocorticoids but not progesterone from rat CBG. The progesterone distribution in the rat plasma was not significantly influenced	Louw and Swart (1999)
	In vivo	Female Wistar rat	Not specified	0.5 ml PBS/day	Unspecified	0.9 mg/day and 40% of the total feed/day)	16 days	Intraperitoneal	Administration of both compound A and S. tuberculatiformis resulted in contraception, characterized by prolonged diestrus. The contraceptive effect was reversible.	
Securidaca longipedunculata Fresen.	In vitro	Human sperm	Chloroform and ethanol	Viagra	Root bark	1, 2.5, 6.5, and 10 mg/ml	48 h	Not applicable	Sperm motility, sperm vitality, and sperm membrane integrity were severely affected after 24 h at a dose of 6.5 mg/ml.	Rakuambo et al. (2006)
Typha capensis (Rohrb.) N.E.Br	In vitro	Human sperm	Water	No control	Rhizome and leaves	1 μg/ml	1 h	Not applicable	The rhizome extract had significant negative effects on vitality, motility, and sperm production.	Henkel et al. (2012)

traditional methods of preventing pregnancy include herbal mixtures, although there has been very little research conducted to document traditional methods used by the different cultural groups in South Africa (Department of Health, Republic of South Africa, 2012). As recorded by Mothiba et al. (2012), the use of herbs to prevent pregnancy was one of the methods used by the community of Capricorn district of Limpopo province, South Africa. Ncube (2012) also reported the use of herbs as contraceptives in Diepsloot, South Africa. Although the Department of Health, Republic of South Africa (2012); Mothiba et al. (2012) and Ncube (2012) reported the use of herbs as contraceptives, the names of the herbs were not specified.

Table 1 illustrates that each of the nine provinces of South Africa is home to at least one or more of the plants used for contraception. In terms of distribution, KwaZulu-Natal had the highest number of plants while Northern Cape was the least represented. Based on the Red List of South African plants (South African National Biodiversity Institute SANBI, 2016), there are no severe threats to most of the identified plant species. Among the recorded plants, 9 have not been assessed and 11 are classified as least concern.

Plant parts of the plant used for contraception include root, leaf, stem, tuber, rhizome, and whole plant (Table 1). The part of the plant part mostly used was the root, while the seeds, tuber, and rhizome were the least used. In South Africa, medicinal plants used for contraception are often taken orally. Oral administration is not the only way medicinal plants are used for contraception in South Africa. For example, women in Diepsloot, South Africa, reported that traditional healers dipped a red string in a mixture of herbs and asked them to tie it around the waist as a contraceptive (Ncube, 2012). Wood and Jewkes (2006) also reported tying a rope containing traditional medicines around the waist as a contraceptive in South Africa. As applicable in South Africa, wearing of medicinal plants around the waist for contraception is well practiced in other African countries such as Malawi (Maliwichi-Nyirenda and Maliwichi, 2010), Nigeria (Jinadu et al., 1997), Uganda (Ntozi and Kabera, 1991), Gambia (Bledsoe et al., 1994), and Mozambique (Agadjanian, 1999).

Some of the medicinal plants used for contraception in South Africa given in Table 1 are mixed with other medicinal plants and taken as concoctions. For example, a decoction of cooked and baked tuber of *Kedrostis nana* is mixed with boiled leafy stems of *Dicerothamnus rhinocerotis* and taken as a contraceptive (Rood, 1994). Furthermore, the root of *Acalypha brachiata* is mixed with the bark of *Kigelia africana* and chopped. A handful of the chopped plant material consisting the root of *A. brachiata* and the bark of *K. africana* is boiled with water just covering the plant material until water drops to the same level of the plant material. The plant material, and cooled before straining. Half a cup of the plant material is taken three times daily to induce lactation by a new mother just after delivery (de Wet and Ngubane, 2014).

In Table 1, no medicinal plant was found to be used by men for contraception in South Africa, including literature on the use of medicinal plants as contraceptives in general. The identified plants are either taken by women or the gender was not specified. For example, Hutchings et al. (1996) indicated that the sap from the leaves of various *Aloe* species is widely used by Zulu women as an oral contraceptive. Water extracts of *Salsola tuberculatiformis* are used by the San women as an oral contraceptive (Swart et al., 2003). The discovery of plant-derived male contraceptives that are both reliable and reversible will help reduce the burden of unwanted pregnancies and risky abortions faced by women (Handelsman, 2005).

In South Africa, herbs are mixed and taken orally for three months before engaging in sexual intercourse so that a woman do not fall pregnant (Mothiba et al., 2012). Traditionally, the Ndebele people of South Africa commonly eat *Flueggea virosa* before intercourse as a contraceptive (Tabuti, 2007). Therefore, the statement by Mothiba et al. (2012) that medicinal plants in South Africa are taken "before sexual intercourse" cannot be taken lightly. No plant was found to be

used after coitus as an emergency contraceptive in South Africa. However, Zimbabwean women drink the powdered roots of *F. virosa* before sexual intercourse to prevent pregnancy (Maroyi, 2013). *Pouzolzia mixta* is taken orally by Zimbabwean women as an infusion or decoction the morning after sexual intercourse to prevent pregnancy and thus may possess postcoital antifertility activity (Sewani-Rusike, 2013).

Some of the identified plants listed in Table 1 as being used for contraception are also used for conception. Among the VhaVenda, *Securidaca longipedunculata* is prescribed to enhance sexual activity in men (Van Wyk et al., 1997). The powdered root is used as an aphrodisiac in the treatment of impotence in Venda (Arnold and Gulumian, 1984). *Typha capensis* is harvested to make decoctions to promote fertility in women and libido in men (Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996). *Schkuhria pinnata* is also used as an aphrodisiac (Deutschlander et al., 2009).

No information pertaining to the traditional use of *B. latifolia, T. capensis,* and *Garcinia livingstonei* as contraceptives was found. The reason could be that focus or emphasis is placed on their aphrodisiac properties. Hutchings et al. (1996) did not specify the *Aloe* species used by the Zulu as an oral contraceptive. The contraceptive activity of *Olea europaea and Olea exasperate* was reported on a university of Western Cape website (http://www.uwc.ac.za.). No published article regarding the contraceptive activity of *Olea europaea* and *Olea exasperate* could be found.

The following plants were simply listed or mentioned as being used for contraception, without any information pertaining to contraceptive use: *Dioscorea dregeana* (Wink and Van Wyk, 2008); *Englerophytum magalismontanum* (Mabogo, 1990); *Leucaena leucocephala* (Dzoyem and Eloff, 2015); *Withania somnifera* (Devi, 1996); *Trachyandra muricata* (Philander, 2011); *Cordia monoica* (Cambie and Brewis, 1997) and *Polygonum aviculare* (Hulley and Van Wyk, 2018).

3.2. Medicinal plants that showed contraceptive activity when evaluated in vivo/in vitro

This section is categorized as studies in males and females that showed contraceptive activity when evaluated *in vivo/in vitro* in South Africa. Table 2 shows medicinal plants that demonstrated contraceptive activity when evaluated either *in vivo* or *in vitro*.

3.2.1. Studies in males

The root bark of *S. longipedunculata* severely affected human sperm motility, sperm vitality, and sperm membrane integrity when evaluated *in vitro*. At 2.5, 6.5, and 10 mg/ml body weight, ethanolic extract of the root bark of *S. longipedunculata* exhibited a decrease in sperm motility. Sperms were nonprogressive and/or moving in random directions. Motility was greatly affected after 24 h of incubation at 2.5 mg/ml and after 4 h at both 6.5 and 10 mg/ml doses. Sperm vitality and membrane integrity were also inhibited (Rakuambo et al., 2006).

Yakubu and Afolayan (2009a) studied the effect of the water extracts of *Bulbine natalensis* stem on the sexual behavior of male rats. Findings indicate that the water extract at 100 mg/kg body weight significantly decreased mount, intromission, and ejaculatory frequencies in male rats. Plant extracts at 100 mg/kg body weight decreased the serum testosterone and progesterone levels (Yakubu and Afolayan, 2009a). The ability of *B. latifolia* to decrease the serum testosterone and progesterone shows contraceptive activity given that rats with low or no sexual activity have lower progesterone and testosterone levels than those displaying the highest sexual performance (Alvarenga et al., 2010).

Henkel et al. (2012) investigated the effect of rhizome and leaf extracts of *T. capensis* on sperm count, motility, and membrane integrity. Treatment of ejaculated human sperm with the water extract of rhizome decreased the values of all sperm parameters measured. Even though the extract showed significant antioxidative activity, a property

known to improve spermatogenesis and steroidogenesis, a decrease in human sperm motility, vitality, and percentage of sperm within mitochondrial membrane potential decreased significantly (Henkel et al., 2012).

3.2.2. Studies in females

Oral and intraperitoneal administration of 2-(4-acetoxyphenyl)-2chloro-N-methyl-ethylammonium chloride (Compound A), an analog of phenylaziridine precursors that occur in S. tuberculatiformis and do not itself occur in the plant, showed a contraceptive effect on female rats, with a concomitant decrease in total body, uterus, and ovary mass and an increase in adrenal mass (Louw et al., 1997). In another study, it was shown that S. tuberculatiformis exerts a contraceptive effect, which was characterized by persistent diestrus in nulliparous female rats and the decrease in the number of estrus days per 16-day period. The contraceptive effect was reversible, as cessation of the administration of test compounds marked a return of the estrous cycle. When evaluated in vivo, administration of both compound A and S. tuberculatiformis resulted in contraception characterized by prolonged diestrus. The contraceptive effect was reversible, as cessation of the administration of test compounds marked a return of the estrous cycle to that in the control animals (Louw and Swart, 1999).

Swart et al. (2003) identified the active substances in *S. tu-bercultatiformis* involved in contraception and the prolonged gestation observed in Karakul sheep. The chemicals in the plant were isolated by solvent partitioning and decomposed under acidic conditions to yield three compounds that included 4-hydroxyacetophenone (1-(4-hydroxy)-ethanone), 4-hydroxy-3-methoxyacetophenone (1-(4-hydroxy)-3-methoxyphenyl)-ethanone), and 4-hydroxybenzaldehyde (Swart et al., 2003). Both water and ethanolic extracts of *P. mixta* roots inhibited implantation at 300 mg/kg body weight when orally administered to female Sprague Dawley rats 7 days before and 10 days after mating (Sewani-Rusike, 2013).

3.3. Safety and toxicity of medicinal plants used for contraception in South Africa

3.3.1. Safety of medicinal plants used as contraceptives in South Africa

The safety of the plant is as important as its efficacy. Medicinal plants used as contraceptives in South Africa are considered safe in general. There is no data that suggested health risks by most plants including *B. latifolia, P. mixta, S. tuberculatiformis, S. longipedunculata,* and *T. capensis* as herbal contraceptives or as medicinal plants in general. However, one of the medicinal plants used for contraception, *D. dregeana,* is reported to be poisonous to humans and monkeys and to make a person mad drunk (Wink and Van Wyk, 2008). The paralytic effect of *D. dregeana* on the central nervous system can lead to human death (Ndhlala et al., 2013).

3.3.2. Toxicity of medicinal plants evaluated in vivo/in vitro

The toxicity of medicinal plants that showed contraceptive activity when evaluated in vivo or in vitro is summarized in Table 3. Histologic examination of rat testes after administration of B. natalensis stem revealed well-preserved seminiferous tubules with normal amount of stroma, normal population of spermatogenic and supporting cells, and normal spermatocytes within the lumen. All indices such as reproduction, maternal, embryo/fetotoxic, teratogenic, and reproductive hormones in the female rats did not show statistically significant difference compared to that of their control except the resorption index, which increased at the dose of 100 mg/kg body weight of the extract. The absence of alterations in the reproductive parameters of female rats at doses of 25 and 50 mg/kg body weight of B. natalensis stem extract suggests that the extract is "safe" for use at these doses by females, whereas the extract dose of 100 mg/kg body weight portends a negative effect on some reproductive functions of male and female rats (Yakubu and Afolayan, 2009b).

: medicinal plants evaluated <i>in vivo</i> or <i>in vitro</i> for contraception in South Africa.	Animal Extract used Control Doses tested Duration Administration Results Reference tested	Mate 1 ml water 25, 50, and 100 mg/ Males (7 days) Female Orally The epididymal sperm count, motility, morphology, and viscosity Yakubu and female rat kg (between 7 and 14 days of pregnancy) the epididymal sperm count, motility, morphology, and viscosity Afolayan (2009b) female rat kg (between 7 and 14 days of pregnancy) treatment. All indices such as reproduction, matemal, embryo, treatugenic, and reproductive hormones in the female rats did not show statistically difference compared to the control except the resorption index.	Mice Water and Normal 2000 and 4000 mg/ Observed over 72 h Orally No behavioral changes and no mortalities were observed in all Sewani-Rusike ethanol saline kg (2013)	Rat Ethanol No control Phase 1 (10, 100, Observed over 24 h Intraperitoneal The crude ethanol extract of S. longipedunculata possessed Ngulde (2013) 1000 mg/kg) 1000 mg/kg) antinociceptive activities, but it was a highly toxic extract in rats Phase 2 (5, 20, and with an intraperitoneal lethal dose (LD ₅₀) value of 14.14 mg/kg.	Rat Water No control Phase 1 (10, 100, and Observed for 24 h Orally A median lethal dose (LD ₅₀) value of 771 mg/kg obtained is an Auwal et al. 1000 mg/kg) indication that the plant is slightly toxic to the experimental (2012) Phase 2 (250, 400, model (albino rats) used. (500, 700, and 850 mg/kg) S50 mg/kg)	Mice Water No control Limit dose of Short term (48 h) Orally The limit dose did not cause any mortality or signs of acute Etuk et al. (2006) 5000 mg/kg Long term (14 days) toxicity in any of the mice tested in the short-term (48 h) and Long term (14 days)
nedicinal plants evaluated <i>in</i>	nimal Extract used Consted	ale and Water 1 m nale rat	ice Water and Noi ethanol sali	tt Ethanol No	t Water No	ice Water No
Table 3 Oxicity studies on some of the n	Species Ar te	Bulbine latifolia (L.f.) Spreng. M. fei	Pouzolzia mixta Solms Mi	Salsola tuberculatiformis Botsch Rɛ	Securidaca longipedunculata Ra Fresen.	Mi

Oral treatment with an extract dose of 300 mg/kg body weight of *P. mixta* for 7 days before and for 10 days after confirmation of mating exhibited postcoital contraceptive effects by inhibiting implantation in female rats. No behavioral changes and no mortalities in all control and treated mice at doses 2000 and 4000 mg/kg body weight extract doses of *P. mixta* were observed during investigation of acute toxicity in mice (Sewani-Rusike, 2013).

The median lethal dose (LD50) of *S. tuberculatiformis* ethanolic extract on rat was determined by administering the extract intraperitoneally in two phases: as 10, 100, and 1000 mg/kg and as 5, 20, and 40 mg/kg. The crude ethanolic extract of *S. longipedunculata* possessed antinociceptive activity, but was a highly toxic extract in rats after an intraperitoneal administration with an lethal dose (LD₅₀) of 14.14 mg/kg (Ngulde, 2013).

The aqueous root bark extract of *S. longipedunculata* was slightly toxic to albino rats, and an lethal dose (LD_{50}) of 771 mg/kg was determined when the extract was orally administered to rats in two phases: as 10, 100, and 1000 mg/kg and as 250, 400, 600, 700, and 850 mg/kg. Pharmacologically, a median lethal dose (LD_{50}) of 771 mg/kg is an indication that the plant is slightly toxic to the experimental model (albino rats) used (Auwal et al., 2012). However, the limit dose of 5000 mg/kg *S. longipedunculata* did not cause any mortality or signs of acute toxicity in any of the female mice tested in the short-term (48 h) and long-term (14 days) observatory days (Etuk et al., 2006). No acute toxicity study for *T. capensis* was found during the review.

4. Conclusions

The current review revealed that there is currently a lack of detailed and comprehensive information about the use of medicinal plants as contraceptives in South Africa. For example, data regarding the use of plants as contraceptives in South Africa do not adequately address plant gender specification, age restrictions, safety and efficacy, plant storage, dosage, reasons for use, and, more importantly, mechanisms of action. The reason could be that research on indigenous contraception in South Africa lacks specialization, with most ethnographic studies focusing on indigenous contraception in general.

Of the 25 medicinal plants identified, only five were found to have contraceptive activity when evaluated *in vivo/in vitro*: *B. latifolia* had an influence on male reproductive hormones; *S. longipedunculata* and *T. capensis* influenced sperm parameters; and *S. tuberculatiformis* prolonged diestrus and *P. mixta* inhibited implantation. *S. longipedunculata* and *T. capensis*, therefore, acted as spermicides, whereas *B. latifolia*, *S. tuberculatiformis*, and *P. mixta* acted as contraceptives.

A literature gap exists on medicinal plants used in South Africa by men for contraception and by women for postcoital contraception. In this review, none of the plants were specified as being traditionally used for male contraception. However, Table 2 details the use of three plants for male contraception: *B. latifolia, S. longipedunculata, and T. capensis. B. latifolia* is traditionally used for conception, whereas *S. longipedunculata* and *T. capensis* are used for both contraception and conception. *B. latifolia* and *T. capensis* showed contraceptive activity when, in fact, the intention was to evaluate conception activity. *B. latifolia* and *T. capensis* thus showed contrasting results.

Furthermore, no medicinal plants were specified to be used for postcoital contraception in South Africa. However, Table 2 illustrates the postcoital contraceptive activity of *P. mixta* when evaluated *in vivo*. Therefore, although there is no evidence of medicinal plants being traditionally used for male contraception or for female postcoital contraception in South Africa, experimental data show that medicinal plants can act as male contraceptives and female postcoital contraceptives.

In-depth ethnobotanical studies are needed in South Africa to investigate medicinal plants traditionally used by males for contraception and by women for postcoital contraception. Documentation of the use of medicinal plants as male contraceptives and as female postcoital contraceptives will assist in the preservation of indigenous knowledge in the country and act as a reference guide for designing *in vivo* and *in vitro* investigations on male and female contraception.

One methodological concern regarding *in vivo* and *in vitro* studies observed is a constant evaluation of only one sex, i.e., either male or female animals were evaluated but not both. An ideal experimental design is one for which a plant (or concoction) is evaluated *in vitro* and *in vivo*, precoitally for male animals and both pre and postcoitally for female animals. The interchangeable use of the terminologies antifertility, family planning, birth control, and contraception creates conceptual challenges and concerns. Scientific identification and isolation of active principles need to be paid attention.

Medicinal plants such as *B. latifolia* show contraceptive activity in male rats by decreasing the serum testosterone and progesterone levels *and P. mixta* that inhibit implantation in female rats without showing any signs of toxicity are potential sources for the discovery and development of safe male hormonal contraceptives and female postcoital hormonal contraceptives. These plants can thus play a reproductive role in addressing teenage pregnancy in South Africa, as well as offering alternative contraception options for couples with health and accessibility challenges associated with modern contraceptives.

However, some of the plants are reported to cause abortion and death in animals or are known to be poisonous to humans. Teenagers and couples wishing to prevent pregnancy through the use of medicinal plants must therefore ensure that the traditional healer consulted is an expert on the use of herbal contraceptives. In addition, traditional healers need to be included when drafting government policies, initiating research projects, revising the curriculum, and developing other social or health interventions on family planning, birth control, and contraception in South Africa. *In vivo, in vitro,* and toxicity studies are needed to ensure that interventions in reproductive health using herbal medicines is safe.

Acknowledgments

This work was supported financially by National Research Foundation (NRF) of South Africa through a Grant (UID: 107748, 2016) to M.A.M. Financial assistance by the North-West University (NWU), Mmabatho, South Africa, is also gratefully acknowledged. The support of the staff at NWU library (Mahikeng campus) is gratefully acknowledged. We also acknowledge the assistance of the Department of Geography and Environmental Sciences at NWU (Mahikeng campus) for providing the map.

Author contributions

M.A. Moroole: Conducted research, contributed to writing, and submitted the final edited manuscript.

S.A. Materechera: Conceptualized the study, contributed to writing, and edited the final draft of the manuscript.

W. Otang Mbeng: Contributed to writing and edited the final draft of the manuscript.

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Declarations of interest

The authors have no conflict of interest.

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