Natural surfactants as potential contraceptive and spermicidal agents

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VAGINAL CONTRACEPTION AND SPERMICIDAL AGENTS

Sameh M. Arab, writing for Arab World Books (www.arabworld-books.com), quotes the Ebers Papryus, an ancient medical manuscript dating from 1550 BCE: “To cause a woman to stop being pregnant, be it one, two or three years: part of acacia, colocynth, dates, finely ground in a hin of honey, fibers are moistened therewith, introduced into her vagina.” She continues: “Contraception was also performed by the insertion of crocodile oil, gum acacia, or honey consperge and natron [Na₂CO₃ ⋅ 10H₂O] into the vagina. Gum Acacia sp. when dissolved produces lactic acid, a very effective known spermicidal.”

Gum of the genus Acacia—A. dealbata, A. longifolia, A. melanoxylon, and A. retinodes—contains phytosteryl glucosides: β-sitosterol, campesteryl and stigmasteryl β-glucoside, spinasterol-3-O-β-D-glucoside, 22,23-dihydrospinasterol-3-O-β-D-glucoside, several glycoside hexabenzoates: 1,3-di-O-galloyl-4,6-(−)-hexahydroxydiphenoyl-β-glucopyranose, 1-O-galloyl-β-glucopyranose, 1,6-di-O-galloyl-β-glucopyranose, 1,3,6-tri-O-galloyl-β-glucopyranose, isorhamnetin 3-O-rutinoside, quercetin 3-O-rutinoside, quercetin 3-O-gentiobioside, quercetin 3-O-glucosylgalactoside, spinasterol-3-O-β-D-glucoside, 22,23-dihydrospinasterol-3-O-β-D-glucoside, several glycoside hexabenzoates: 1,3-di-O-galloyl-4,6-(−)-hexahydroxydiphenoyl-β-glucopyranose, 1-O-galloyl-β-glucopyranose, 1,6-di-O-galloyl-β-glucopyranose, 1,3,6-tri-O-galloyl-β-glucopyranose, isorhamnetin 3-O-rutinoside, quercetin 3-O-rutinoside, quercetin 3-O-gentiobioside, quercetin 3-O-glucosylgalactoside, quercetin 3-O-glucoside and quercetin 3-O-galactoside, and flavonoids quercetin 3-O-β-D-glucoside, quercetin 3-O-β-D-glucoside, quercetin 3-O-β-D-glucoside, quercetin 3-O-rutinoside, myricetin 3-O-β-D-glucoside and myricetin 3-O-β-D-glucoside, and taxifolin 7-O-α-D-glucoside. All phytosterol glucosides are known as spermicidal agents. Ancient Egyptian women developed a tampon-like object that contained lactic acid anhydride, a major ingredient in modern contraceptive jellies.

Neem oil is a good spermicidal agent. Extracted from the seeds of Azadirachta indica, it contains 9-hexadecenoic, palmitic, heptadecanoic, linoleic, oleic, stearic, 11-eicosenoic, eicosanoic, docosanoic, and tetracosanoic acids, with oleic acid having the highest content, at 43.2%; and sitosterol, stigmasterol, campesterol, fucosterol, and also as water-soluble compounds in glycoside form as well as acyclic norditerpene 2,6,10,14-tetramethyl pentadeca-8-en-2,7-β-diol (azadirechterminol A), a monocyclic homoditerpene 2,6,10-trimethyl-14-cyclopent-15-enyl-O-tetradecan-6x,8α-diol (azadirterpinol B), and 2-octadecanoic acid-4-palmityl acid-2,4-pentanediyl ester.

Cottonseed oil (palmitic [23%], oleic [18%], linoleic [53%], and 10% mixture of arachidic, behenic, and lignoceric acids) and kaempferol and quercetin 3-O-neohesperidosides as major glycosides have also been found to act as good spermicidal agents. Creams, gels, foams, and suppositories containing these oils (as major ingredients) have been used for vaginal contraception. The vaginal spermicidal agents work in two different ways to prevent pregnancy. Their insertion in the vagina before intercourse produces a barrier to sperm penetration of the cervical os (opening to the uterus), and the active ingredients are directly toxic to sperm. All modern spermicidal agents contain the active ingredient nonoxynol 9 (p-nonylphenol decaethylenyl glycol ether), which immobilizes and kills sperm on contact.

Morrhuc acid is a mixture of fatty acids occurring in cod liver oil (codfish: Gadus morrhua). It is a more effective vaginal contraceptive (as major ingredient) than nonoxynol 9. Morrhuc acid contains the unsaturated fatty acids docosahexaenoic (C22:6), eicosapentaenoic (C20:5), arachidonic (C20:4), linoleic (18:2), tetracosanoic, docosapentaenoic, linolenic (C18:3), and oleic (C18:1) acids. The spermicidal activity of C22:6 was the greatest, followed by C20:5, C20:4, C18:3, C18:2, and C18:1 in decreasing order, indicating that the spermicidal activity increased with increasing degree of unsaturation. Emulsions and sodium salts of morrhuic acid...
and its component unsaturated acids all show a high spermicidal activity. Several individual water-soluble (as glycosides) spermicidal agents have been isolated from medicinal plants and marine species (Fig. 1). Thus, sophorolipids are extracellular glycolipids produced by Candida bombicola ATCC 22214 when grown in the presence of glucose and fatty acids. These compounds have a disaccharide head group connected to a long-chain hydroxyl-fatty acid by a glycosidic bond. Sophorolipids (Fig. 1A: compounds 1–8) are strong spermicidal agents, and also show antibacterial and antiviral activities.

Two spermicidal saponins ardisioside A (9) and B (10) (Fig. 1B) isolated from Ardisia neriifolia were characterized as primulagenin A-3-O-[α-D-galactopyranosyl(1→4)-α-L-rhamnopyranoside and primulagenin A-3-O-[α-D-galactopyranosyl(1→2)-α-L-arabinopyranosyl(1→4)-α-L-rhamnopyranoside, respectively. Bivittoside D (Fig. 1C: 11) is a unique triterpenoid saponin isolated from the sea cucumber Bohadschia viensis that has been used for its potent spermicidal and fungicidal activity.

The antiovulatory, anti-implantation, abortifacient, fetus-absorption, uterine-stimulant, spermicidal, semen-coagulant, and antispermatogenic activity of different plants extracts have been known for several decades. Aristolic acid, butin, embelin, plumbagin, and solasodine—isolated from Aristolochia indica, Butea monosperma, Embelia ribes, Plumbago zeylenica, and Solanum xanthocarpum, respectively—have the potential for being both male and female contraceptives. Salannin, a limonoid bitter principle of the seed oil of Azadirachta indica, shows a high spermicidal activity. Spermicidal agent stepharine has been isolated from leaves and fruits of Sri Lankan Diplocrisia glaucescens (Menispermaceae). 1,2-Benzisothiazole derivatives show strong spermistatic and spermicidal activity and can be included in vaginal creams, gels, foams, and suppositories at concentrations of 0.1–1% for use as contraceptives.

**FIG. 1B-1C.** Natural spermicidal agents isolated from medicinal plants and marine species.
ORAL CONTRACEPTIVE AGENTS

Oral contraceptives have been available for more than 4,000 years. Women in ancient China drank mercury to prevent pregnancy. Traditional Chinese medicine describes several liquid syrups that were used as oral contraceptives. These liquid syrups were manufactured from (parts by wt.): carrot seed volatile oil (120–160), Polygonum japonicum (80–110), Sophora japonica (60–100), Pseudolarix amabilis (50–80), Radix et Rhizoma Rhei (50–80), Platycladus orientalis (40–70), Pericarpium zanthoxyli (40–70), and menthol. The petal extract of Urhul (also known Chinese shoe flower), Hibiscus rosasinensis, is known as the allopathic oral conventional female contraceptive. Women in India imbibed carrot seeds (carrot seed oil is the essential oil extract of seed from the carrot plant Daucus carota, containing luteolin 3′-O-β-D-glucopyranoside, and luteolin 4′-O-β-D-glucopyranoside). This long-acting oral contraceptive is effective for four months and contains a mixture of dry extracts: Embelia ribes, Piper betel, P. longum, Asafoetida, oil of Polianthes tuberosa, and Abrus precatorius.

In ancient Greece and Rome, the juice of the silphium plant (also known as silphion or laser, Ferula asafoetida) was a popular and effective form of oral contraceptive, which women took once a month. The folk medicine asafoetida (oleo-gum-resin obtained from Ferula plants) contained 14–17% volatile oils, comprising: α- and β-pinene, diallyl sulfate, diallyl sulfide, diallyl disulfide, secondary butyl propenyl disulfide, α-phellandrene, geranyl acetate, ferulic acid, and umbelliferone.

The fruits of ajowan (Trachyspermum ammi) cultivated in Iran and harvested at the pasty (unripe) stage contain as major components γ-terpinene (43%), thymol (32%), and p-cymene (21%). Peppermint oil (palmitic, oleic, linoleic, linolenic, and azobenzene-4-carboxylic acids) from Mentha piperita (Lamiaceae) is one of the medicinal and aromatic plants whose essential oil is widely used in the medicinal, food, cosmetic, and health industries. Ajowan and peppermint oils, which are major ingredients of soft drinks, have been used for oral contraception in Iran, Iraq, and other countries. Zoapatle aqueous crude extract from Montanoa tomentosa has been used as an oral contraceptive in traditional Mexican medicine for centuries. The individual kaurenoic acid, the methyl esters of 15-hydroxy-dihydro-kaurenoic and 15-keto-dihydro-kaurenoic acids isolated from M. tomentosa were six times more potent than verapamil (a female contraceptive) at the same concentration.

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