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Potential Value of Plants as Sources of New Antifertility Agents II *

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Keyphrases □ Antifertility agents—review of plant sources, classified by anatomical mechanism and folkloric route of administration □ Medicinal plants—sources of antifertility agents, classified by anatomical mechanism and folkloric route of administration, review □ Plant extracts—potential sources of antifertility agents, review □ Contraceptives—plants with active constituents, review □ Abortifacients—plants with active constituents, review □ Oxytocics—plants with active constituents, review □ Estrogenic plants—review of active principles

CONTENTS

ESTROGENIC PLANTS AND THEIR ACTIVE PRINCIPLES

Historically, a number of plants have been used as sex hormones in native medicine. The pomegranate, *Punica granatum* (Punicaceae), was a symbol of immortality, fertility, and love in Oriental religions, and its legendary powers date back to Greek and Judeo-Christian mythology (921). In Egypt, the pollen grains of the date palm, *Phoenix dactylifera* var. *samani* (Palmae), were used to induce fertility in women; while moghat, *Clossostemon brugieri* (Sterculiaceae), is used as a postpartum hot beverage (922).

Phytochemical interest in plant estrogens, however, remained relatively dormant until the 1950's. The increased interest in phytoestrogens was, according to Biggers (923), due to at least four factors:

1. The recognition that infertility in animals and humans could follow excessive ingestion of plants rich in compounds possessing estrogenic activity.
2. The known existence of "spring flush" (increased yield of improved milk) in dairy cattle ingesting certain rapidly growing grasses that contained estrogenic substances.
3. The possibility that the demonstrated improvement in carcass quality, produced by the feeding of synthetic estrogens, might also be able to be produced by the feeding of plants rich in estrogens.
4. The possibility of obtaining estrogenic substances economically from plant sources.

The occurrence of substances in plants capable of inducing animal estrus was first demonstrated by Dohrn *et al.* (924) in 1926. The first isolation of an estrogen from plants was reported by Butenandt and Jacobi (925) in 1933, when they succeeded in isolating 18 mg of estrone from 50 kg of a botanically unspecified palm kernel press cake. In the same year, Skarzynski (926) reported on the isolation of 7.5 mg of estriol from 65 kg of female willow catkins. Thirty years elapsed before any concerted efforts were made in the phytochemical investigation of these compounds. Jacobsohn *et al.* (927), in 1965, raised the question as to the validity of claims for the presence of estrogens in plants when they failed to isolate estrone from any of four geographic varieties of the African oil palm, *Elaeis guineensis* (Palmae). *E. guineensis* may or may not have been the plant investigated by Butenandt and Jacobi (925), although by deductive reasoning Bradbury and White (928) thought that it certainly must have been.

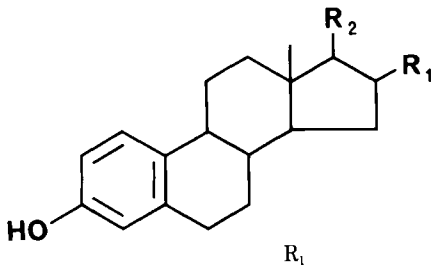
The question of the presence of estrogenic hormones in plants raised by Jacobsohn *et al.* (927) has been answered by work since 1965. The date palm, *P. dactylifera* var. *khadrawy* (Palmae), was

Editor's note: Part I of this article appeared in the April 1975 issue of the *Journal of Pharmaceutical Sciences*.

Table VI—Occurrence of Steroid Estrogens in Plants

Plant Name	Steroid Estrogen	Reference
Chenopodiaceae		
Beta vulgaris	β-Sitosterol[a] (CXLII)	1035–1037
Gramineae		
Avena sativa	Estrone (CLVIII)	1038
Oryza sativa	Estrone	1038
Triticum aestivum	Estrone	1038
Leguminosae		
Glycyrrhiza glabra	β-Sitosterol	1035–1037
	Estriol (CLVII)	1039
Phaseolus vulgaris	Estrone	1040
	Estriol	1040
	17α-Estradiol (CLV)	1040
Palmae		
Elaeis guineensis	Estrone	925
Hyphaene thebaica	Estrone	1041
Phoenix dactylifera	Estrone	929, 1042–1045
Phoenix dactylifera var. *samani*	Estrone	922
Punicaceae		
Punica granatum var. *nana*	Estrone	1046, 1047
Rosaceae		
Malus sylvestris	Estrone	1048
Salicaceae		
Salix caprea	Estrone	926
Sterculiaceae		
Clossostemon bruguieri	Estrone	922

[a] β-Sitosterol is a ubiquitous substance in plants, and no attempt has been made to document those plants in which it has been reported present. The plants indicated apparently contain a high enough percentage so that extracts exhibit estrogenic activity.



	R_1	R_2
CLV: 17α-estradiol	H	---OH
CLVI: 17β-estradiol	H	—OH
CLVII: estriol	---OH	—OH
CLVIII: estrone	H	=O

Structures of Estrogenic Sterols

demonstrated to contain estrone (CLVIII) by TLC; subsequently, the compound was isolated (929). A number of estrogenic sterols have since been reported as being derived from higher plants. A list of these compounds and their plant sources is presented in Table VI. A review of steroid estrogens in plants is available (921).

Biological and chemical interest in nonsteroidal estrogenic substances was spurred by the work of Bennetts and his coworkers (930, 931), who reported in 1946 that the serious decline in lambing rates in Australia was due to their grazing on the Dwalganup strain of subterranean clover *(Trifolium subterraneum)*, and the subsequent isolation of the isoflavone, genistein (CXCIII), from this plant (932). This compound was later demonstrated to be estrogenic (933). Since then, other isoflavones having estrogenic activity have been found in various forage plants and studies of environmental factors on the isoflavonoid content of these plants have been made (934–958). A large reduction in sperm numbers was observed on prolonged grazing of sheep on clover pasture (959); it is not known if this activity is also due to the estrogenicity of clover pastures. A list of estrogenic and potential estrogenic isoflavones and their sources is presented in Table VII.

In addition to the steroids and isoflavones, another group of chemical compounds found in forage plants that have estrogenic activity are the coumestans, having the skeletal structure of 6*H*-benzofuran(3,2-*c*)benzopyran-6-one. The best known compound in

Table VII—Plants Containing Isoflavonoids

Plant Name	Isoflavonoid	Reference
Amaranthaceae		
Iresine celosioides	Tlatlancuayin (CCXLVIII)	1049
Gramineae		
Bromus mollis	Genistein (CXCIII)	1050
Cynodon dactylon	Daidzein (CLIX)	1051
	Genistein	1051
Hyparrhena filipendula	Daidzein	1051
	Genistein	1051
Setaria ciliolata	Daidzein	1051
	Genistein	1051
Triticum aestivum	Genistein	1050
Iridaceae		
Belamcanda chinensis	Tectorigenin 7-*O*-glucoside (CCXXVI)	1052, 1053
Iris sp.	Irigenin 7-*O*-glucoside	1064
	Tectorigenin 7-*O*-glucoside	1064
Iris florentina	Irigenin (CCXXXIX)	1054
	Irigenin 7-*O*-glucoside (CCXL)	1055, 1056
	Irilone 4′-*O*-glucoside (CCXXVIII)	1057
	Irisflorentin (CCXLIX)	1054
	Irisolone (CCXXX)	1054
	Irisolone 4′-*O*-bioside (CCXXIX)	1057

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
	Iristectorigenin B (CCXXXVI)	1054
Iris germanica	Homotectoridin (CCXVII)	1058
	Irigenin 7-*O*-glucoside	1056
	Irilone (CCXXVII)	1059
	Tectorigenin 7-*O*-glucoside	1058
Iris nepalensis	Irisolidone (CCXXXV)	1060
	Irisolone	1061
Iris pallida	Irigenin 7-*O*-glucoside	1056
Iris tectorum	Irigenin 7-*O*-glucoside	1062
	Tectorigenin 7-*O*-glucoside	1062–1064
Leguminosae		
Adenocarpus complicatus	Genistein 7-*O*-glucoside (CXCV)	1065
Adenocarpus foliolosus	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein (CCII)	1066
Afrormosa elata	Afrormosin (CXC)	1067
Amphimas pterocarpioides	Afrormosin	1068
Andira parviflora	Biochanin A	1069
	5,7-Dihydroxy-4′-methoxyisoflavone (CCLXXXI)	1069
Astragalus austriacus	Biochanin A 7-*O*-glucoside (CCIV)	1070
Baphia nitida	Santal (CCXIII)	1071, 1072
Baptisia arachnifera	Afrormosin	1073
	Afrormosin 7-*O*-glucoside (CXCI)	1073
	Calycosin (CLXXVII)	1073
	Calycosin 7-*O*-glucoside (CLXXVIII)	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside (CLX)	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside (CLXIV)	1073
	Formononetin 7-*O*-rhamnoglucoside (CLXV)	1073
Baptisia australis	Afrormosin	1073–1075
	Afrormosin 7-*O*-glucoside	1073–1075
	Daidzein	1073, 1074
	Formononetin	1073–1075
	Formononetin 7-*O*-glucoside	1073–1075
	Genistein	1074
	Orobol (CCX)	1074
	Pseudobaptigenin (CLXXX)	1074
	Texasin (CLXXXVIII)	1073, 1076
	Texasin 7-*O*-glucoside (CLXXXIX)	1073, 1074
Baptisia bracteata	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Calycosin	1073
	Calycosin 7-*O*-glucoside	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
Baptisia calycosa	Biochanin A	1073
	Biochanin A 7-*O*-rhamnoglucoside (CCV)	1073
	Calycosin	1073
	Daidzein	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
	Genistein	1073
	Genistein 7-*O*-rhamnoglucoside (CXCVIII)	1073
	Orobol	1073
	Orobol 7-*O*-rhamnoglucoside (CCXII)	1073
Baptisia cinerea	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Calycosin 7-*O*-glucoside	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
	Genistein	1073
	Genistein 7-*O*-glucoside	1073
	Orobol	1073
	Orobol 7-*O*-glucoside (CCXI)	1073
Baptisia hirsuta	Biochanin A	1073
	Biochanin A 7-*O*-rhamnoglucoside	1073
	Genistein	1073
	Genistein 7-*O*-rhamnoglucoside	1073
	6-Hydroxygenistein (CCXXIII)	1073, 1077

(continued)

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
	6-Hydroxygenistein 7-*O*-rhamnoglucoside (CCXXIV)	1073, 1077
	Orobol	1073
	Orobol 7-*O*-rhamnoglucoside	1073
	Pseudobaptigenin	1073
	Pseudobaptigenin 7-*O*-rhamnoglucoside (CLXXXII)	1073
Baptisia lanceolata	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Calycosin	1073
	Calycosin 7-*O*-glucoside	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Genistein	1073
Baptisia lecontei	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Calycosin	1073, 1077
	Calycosin 7-*O*-glucoside	1073, 1077, 1078
	Calycosin 7-*O*-rhamnoglucoside (CLXXIX)	1073, 1077, 1078
	Daidzein	1073, 1078
	Daidzein 7-*O*-glucoside	1073, 1078
	Daidzein 7-*O*-rhamnoglucoside (CLXI)	1073, 1078
	Formononetin	1073, 1078
	Formononetin 7-*O*-glucoside	1073
	Genistein	1073, 1078
	Genistein 7-*O*-glucoside	1073
	Genistein 7-*O*-rhamnoglucoside	1073, 1078
	Genistein 7-*O*-rutinoside (CXCIX)	1078
	Orobol	1073, 1078
	Orobol 7-*O*-rhamnoglucoside	1073, 1078
	Pseudobaptigenin	1073, 1078
Baptisia leucantha	Orobol	1073
	Orobol 7-*O*-glucoside	1073
	Orobol 7-*O*-rhamnoglucoside	1073
Baptisia leucophaea	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Calycosin	1073
	Calycosin 7-*O*-glucoside	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Genistein	1073
	Genistein 7-*O*-glucoside	1073
	Orobol	1073
	Orobol 7-*O*-glucoside	1073
Baptisia megacarpa	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Afrormosin 7-*O*-rhamnoglucoside (CXCII)	1073
	Calycosin	1073
	Calycosin 7-*O*-glucoside	1073
	Calycosin 7-*O*-rhamnoglucoside	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Daidzein 7-*O*-rhamnoglucoside	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
	Formononetin 7-*O*-rhamnoglucoside	1073
	Genistein	1073
	Genistein 7-*O*-glucoside	1073
	Orobol	1073
Baptisia nuttalliana	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Calycosin	1073
	Daidzein	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
	Genistein	1073
	Genistein 7-*O*-glucoside	1073
	Orobol	1073
	Orobol 7-*O*-glucoside	1073
	Tectorigenin (CCXXV)	1073
	Tectorigenin 7-*O*-glucoside	1073
Baptisia perfoliata	Afrormosin	1073
	Calycosin	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
	Orobol	1073
	Orobol 7-*O*-rhamnoglucoside	1073
Baptisia simplicifolia	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Afrormosin 7-*O*-rhamnoglucoside	1073
	Calycosin	1073
	Calycosin 7-*O*-glucoside	1073
	Calycosin 7-*O*-rhamnoglucoside	1073
	Daidzein	1073
	Daidzein 7-*O*-glucoside	1073
	Daidzein 7-*O*-rhamnoglucoside	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
	Formononetin 7-*O*-rhamnoglucoside	1073
Baptisia sphaerocarpa	Biochanin A	1073
	Biochanin A 7-*O*-rhamnoglucoside	1073
	Formononetin	1073
	Formononetin 7-*O*-glucoside	1073
	Genistein 7-*O*-rhamnoglucoside	1073
	Genistein 7-*O*-rutinoside	1073
	Orobol 7-*O*-rhamnoglucoside	1073
Baptisia tinctoria	Afrormosin	1073
	Afrormosin 7-*O*-glucoside	1073
	Biochanin A	1073
	Biochanin A 7-*O*-rhamnoglucoside	1073
	Genistein	1073
	Genistein 7-*O*-rhamnoglucoside	1073
	Orobol	1073
	Orobol 7-*O*-rhamnoglucoside	1073
	Pseudobaptigenin	1073
	Pseudobaptigenin 7-*O*-glucoside (CLXXXI)	1079–1081
	Pseudobaptigenin 7-*O*-rhamnoglucoside	1073
	Tectorigenin	1073
Calycotome spinosa	Genistein	1066
	5-*O*-Methylgenistein	1066
Calycotome villosa	Genistein	1066
	5-*O*-Methylgenistein	1066
Castanospermum australe	Afrormosin	1082
	Formononetin	1082
Chamaecytisus albus	Genistein	1066
Chamaecytisus smyrnaeus	Genistein	1066
	Daidzein	1066
Chamaespartium sagittale	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Chronanthus biflorus	Genistein	1066
	5-*O*-Methylgenistein	1066
Cicer arietinum	Biochanin A	1083–1094
	Biochanin A 7-*O*-glucoside	1095
	Daidzein	1091
	Formononetin	1083, 1085, 1088, 1092–1094, 1096–1099
	Homoferreirin (CCLXXXIV)	1099
	Pratensein (CCXIV)	1100
Cladrastis luteus	Afrormosin	1101
	Cladrastin (CCXVIII)	1101
	Cladrin (CLXXXIII)	1101
	Formononetin	1101
Cladrastis platycarpa	Fujikinetin (CCXX)	1102, 1103
	Fujikinin (CCXXI)	1103
Cordyla africana	6,7-Dimethoxy-3′,4′-methylenedioxyisoflavone (CCXXII)	1104
	6,7,2′,4′,5′-Pentamethoxyisoflavone (CCXLVII)	1104
	6,7,3′,4′-Tetramethoxyisoflavone (CCXIX)	1104
	6,7,3′-Trimethoxy-4′,5′-methylenedioxyisoflavone (CCXLVI)	1104
	Milldurone (CCXLIV)	1104
Cytisus battandieri	Daidzein	1066
	Genistein	1066
Cytisus commutatus	Daidzein	1066
	Genistein	1066
Cytisus eriocarpus	Genistein	1066
Cytisus laburnum	Genistein	1105
	5-*O*-Methylgenistein	1105, 1106
Cytisus proliferus	Daidzein	1066

(*continued*)

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
	Formononetin	1066
	Genistein	1066
Cytisus purgans	Daidzein	1066
	Genistein	1066
Cytisus scoparius	Genistein	1066
Cytisus welwitschii	Daidzein	1066
	Genistein	1066
Dalbergia barrentoana	Caviunin	1107
	Formononetin	1107
Dalbergia ecastophyllum	Daidzein	1108, 1109
	Formononetin	1108, 1110
Dalbergia lanceolaria	Biochanin A 7-*O*-apiosylglucoside (CCVII)	1111
	Pseudobaptigenin	1112
Dalbergia nigra	Caviunin (CCXXXVII)	1113
Dalbergia paniculata	Biochanin A	1114
	Caviunin	1115
	Dalpatein (CCXLII)	1115
	Dalpatin (CCXLIII)	1116
	Formononetin	1114
	Paniculatin (CCLXXIII)	1114
Dalbergia retusa	Retusine (CLXX)	1117
	8-*O*-Methylretusine (CLXXI)	1117
Dalbergia riparia	Afrormosin	1118
	Caviunin	1118
	Caviunin 7-*O*-glucoside (CCXXXVIII)	1118
	Fujikinetin	1118
	Tectorigenin	1118
	Tectorigenin 7-*O*-glucoside	1118
Dalbergia sisso	Biochanin A	1119
	Biochanin A 7-*O*-glucoside	1120
	7,4′-Dimethyltectorigenin (CCXXXIV)	1121
	7-*O*-Methyltectorigenin (CCXXXI)	1119
	7-*O*-Methyltectorigenin 4′-*O*-rhamnoglucoside (CCXXXII)	1122
	Tectorigenin	1119
Dalbergia villosa	Caviunin	1107
Dalbergia violacea	Di-*O*-methyldaidzein (CLXVIII)	1123
	Violanone (CCLXXXV)	1124
Derris malaccensis	Toxicarolisoflavone (CCLXV)	1125, 1126
Derris robusta	Derrubone (CCLII)	1127
	Derrustone (CCXVI)	1127
	Robustone (CCLVIII)	1127
	Robustone methyl ether (CCLIX)	1127
Derris scandens	Chandalone (CCLXXII)	1128
	Osajin (CCLXX)	1129
	5-*O*-Methylosajin (CCLXXI)	1129
	Scandenone (CCLX)	1128, 1129
	Scandinone (CCLXVIII)	1129
Erinacea anthyllis	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Ferreirea spectabilis	Biochanin A	1130
	Ferreirin (CCLXXXIII)	1130, 1131
	Homoferreirin	1130, 1131
Genista acanthoclada	Daidzein	1066
	Genistein	1066
Genista aetnensis	Daidzein	1066
	Formononetin	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista albida	Daidzein	1066
	Genistein	1066
Genista anglica	Daidzein	1066
	Genistein	1066
Genista arsitata	Daidzein	1066
Genista baetica	Daidzein	1066
Genista capitellata	Daidzein	1066
Genista carpetana	Daidzein	1066
Genista cinerea	Daidzein	1066
Genista corsica	Daidzein	1066
Genista cupanii	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista falcata	Daidzein	1066
Genista florida	Daidzein	1066
Genista hirsuta	Daidzein	1066
Genista hispanica	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
Genista hystrix	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista germanica	Daidzein	1066
Genista lobelii	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista lydia	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista micrantha	5-*O*-Methylgenistein	1066
Genista morisii	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista nissana	Daidzein	1066
	Formononetin	1066
Genista obtusirama	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista pilosa	Daidzein	1066
Genista pumila	Daidzein	1066
Genista radiata	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista raetum	Genistein 7-*O*-glucoside	1132
Genista salzmanii	Daidzein	1066
	Formononetin	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista scorpius	Genistein	1066
Genista sericea	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista sessilifolia	Daidzein	1066
	Formononetin	1066
	Genistein	1066
Genista spartioides	Genistein	1066
Genista subcapitata	Daidzein	1066
	Formononetin	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista teritifolia	Daidzein	1066
	Formononetin	1066
Genista tinctoria	Daidzein	1066
	Genistein	1066
	Genistein 7-*O*-glucoside	1066, 1133, 1134
Genista triacanthos	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista tridens	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista ulicina	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Genista umbellata	Daidzein	1066
Genista valentina	Daidzein	1066
Genista villarsii	Daidzein	1066
	Formononetin	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Gleditschia triacanthos	Biochanin A	1135, 1136
Glycine max	Daidzein	995, 1137–1139
	Daidzein 7-*O*-glucoside	1099, 1139–1144
	Genistein	995, 1032, 1139, 1140, 1143, 1145, 1146
	Genistein 7-*O*-glucoside	995, 1032, 1145
	Glycitein (CLXXXVII)	1147
	6,7,4′-Trihydroxyisoflavone (CLXXXVI)	1148–1150
	Isoflavonoids	1151
Glycyrrhiza echinata	Formononetin	1152
Glycyrrhiza glabra	Formononetin	1153, 1154
Laburnum anagyroides	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Lathyrus montanus	Orobol	1156
Lupinus sp.	Genistein	1161
Lupinus luteus	Luteone (CCLI)	1157
Lupinus polyphyllus	Genistein	1158

(continued)

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
	Genistein 7-*O*-glucoside	1159
Lupinus termis	Biochanin A	1160
Lygos monosperma	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Lygos raetam	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Maackia amurensis	Pseudobaptigenin	1162
	Sophorol (CCLXXXVIII)	1163, 1164
Maackia amurensis var. *Buergeri*	7′,4-Dihydroxy-3′-methoxyisoflavone (CLXXVI)	1165
	Formononetin	1165
	Genistein	1165
Machaerium villosum	7′,4-Dihydroxy-3′-methoxyisoflavone	1166
	Formononetin	1166
	Isoformononetin (CLXII)	1166
	7,3′,4′,Trihydroxyisoflavone (CLXXV)	1166
Medicago sativa	Biochanin A	1167–1169
	Daidzein	1167, 1168, 1170–1172
	Formononetin	1167, 1168, 1170–1173
	Genistein	1167–1169
Milletia auriculata	Auriculatin (CCLXI)	1174
	Auriculin (CCLXII)	1175
	Isoauriculatin (CCLXIV)	1175
Milletia dura	Durlettone (CLXIX)	1176
	Durmillone (CCLXVI)	1176
	Milldurone	1176
Milletia ferruginea	Durmillone	1177
	Ferrugone (CCLXXV)	1177
Mundulea sericea	Mundulone (CCLXXVII)	1178
	Munetone (CCLXXXVI)	1179, 1180
Mundulea suberosa	Munetone	1181, 1182
Myrocarpus fastigiatus	Afrormosin	1183, 1184
	Cabreuvin (CLXXXIV)	1183
Myroxylon balsamum	Afrormosin	1184
	Cabreuvin	1183
Neorautanenia amboensis	Dehydroneotenone (CCLVI)	1185
	Neotenone (CCLV)	1185
	Pachyrrhizin (CCLVII)	1185, 1186
Neorautanenia edulis	Dehydroneotenone	1185
	Neotenone	1185
	Pachyrrhizin	1185, 1186
Pterocarpus dalbergioides	Calycosin	1214
Pterocarpus erinaceous	Pseudobaptigenin	1068
Pterocarpus indicus	Formononetin	1215
Pterocarpus osun	Prunetin	1216
Pterocarpus santalinus	Santal	1072, 1217, 1218
Pterocarpus vidalianus	Formononetin	1145
Pterodon pubescens	Milldurone	1206, 1219, 1220
	6,7,2′,3′,4′-Pentamethoxyisoflavone	1206, 1219, 1220
	6,7,3′,4′-Tetramethoxyisoflavone	1206, 1219, 1220
Pueraria mirifica	Miroestrol (CCLXXVIII)	1221, 1222
	Unknown isoflavone	1223
Pueraria pseudohirsuta	Puerarin (CLXXII)	1224
	Puerarin xyloside (CLXXIV)	1224
Pueraria thomsoni	Puerarin	1224
Pueraria thunbergiana	Daidzein	1224–1227
	Daidzein 7-*O*-glucoside	1227
	Genistein	1226
	Puerarin	1224, 1225, 1227
	Puerarin xyloside	1224, 1227
Pueraria tuberosa	Daidzein	1228
	Puerarin	1228
	Puerarin 4′,6″-diacetate (CLXXIII)	1228
Sarothamnus scoparius	Genistein 7-*O*-glucoside	1159
Sophora japonica	Genistein	1229–1232
	Genistein 4′-*O*-glucoside (CXCIV)	1064, 1230–1235
	Genistein 7-*O*-neohesperidoside (CXCVI)	1236
	Genistein 4′-*O*-rhamnoglucoside (CXCVII)	1233–1235
	Genistein 7-*O*-rhamnoglucoside	1230, 1237, 1238
Neorautanenia pseudopachyrrhiza	Dehydroneotenone	1186
	Neotenone	1186
	Nepseudin (CCLIV)	1186
	Pachyrrhizin	1185, 1186
Ononis spinosa	Formononetin 7-*O*-glucoside	1140, 1141, 1187–1191
Orobus tuberosus	Orobol 7-*O*-glucoside	1156, 1192
Ougeinia dalbergioides	Dalbergioidin (CCLXXXII)	1193, 1194

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
	Homoferreirin	1195
	Ougenin (CCLXXXVII)	1193–1195
Pachyrrhizus erosus	Dehydroneotenone	1186
	Neotenone	1186
	Pachyrrhizin	1196, 1197
Pericopsis sp.	Afrormosin	1198
	Formononetin	1198
Phaseolus aureus	Daidzein	1092, 1199
	7,2′,4′-Trihydroxyisoflavone (CCXLI)	1200
Piscidia erythrina	Ichthynone (CCLXVII)	1201
	Jamaicin (CCLXIII)	1202, 1203
	Piscerythrone (CCL)	1204
	Piscidone (CCLXXIV)	1204
Pisum sativum	Isoflavones	1205
Platymiscium praecox	Texasin	1206, 1207
Poecilanthe parviflora	5,7,4′-Trihydroxy-2′,3′-dimethoxy-isoflavanone (CCLXXXVI)	1208
	Mixture of isoflavones	1208
Psoralea esculenta	Isoflavones	1209
Psoralea rigida	Isoflavones	1209
Psoralea scaposa	Isoflavones	1209
Pterocarpus angolensis	7-*O*-Methyltectorigenin	1210
	Muningin (CCXXXIII)	1211, 1212
	Prunetin	1212, 1213
	Sophorol	1163
Sophora subprostrata	Daidzein	1239
	Genistein	1240
Stauracanthos genistoides	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Teline canariensis	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Teline congesta	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Teline linifolia	Genistein	1066
Teline monspessulana	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Teline rosmarinifolia	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Teline spachiana	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Teline stenopetala	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Tephrosia maxima	Maxima substance A (CCXV)	1241
	Maxima substance B (CLXXXV)	1242, 1243
	Maxima substance C (CCLIII)	1244
Tipuana tipu	Formononetin	1245
Trifolium alpestre	Biochanin A	1246
	Formononetin	1246, 1247
	Formononetin 7-*O*-glucoside	1246, 1247
	Genistein	1246
Trifolium anatolicum	Formononetin	1246
	Formononetin 7-*O*-glucoside	1246
	Genistein	1246
Trifolium baccarini	Biochanin A	1246
	Formononetin	1246
	Formononetin 7-*O*-glucoside	1246
	Genistein	1246
Trifolium batmanicum	Biochanin A	1248
	Formononetin	1248
	Genistein	1248
Trifolium campestre	Genistein	1249
Trifolium eriosphoerum	Biochanin A	1246, 1248
	Formononetin	1246, 1248
	Formononetin 7-*O*-glucoside	1246
	Genistein	1248
Trifolium globosum	Biochanin A	1246, 1248
	Formononetin	1246, 1248
	Formononetin 7-*O*-glucoside	1246
	Genistein	1248, 1249
Trifolium hybridum	Biochanin A 7-*O*-glucoside	1250
	Formononetin 7-*O*-glucoside	1250
	Genistein 7-*O*-glucoside	1250

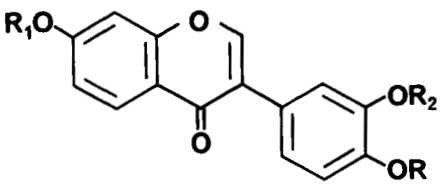
(*continued*)

Table VII—(*Continued*)

Plant Name	Isoflavonoid	Reference
Trifolium incarnatum	Biochanin A 7-*O*-glucoside	1250
	Formononetin 7-*O*-glucoside	1250, 1251
	Genistein 7-*O*-glucoside	1250
Trifolium isodon	Biochanin A	1246
	Formononetin	1246
	Formononetin 7-*O*-glucoside	1246
Trifolium israeliticum	Biochanin A	945, 1246, 1248
	Formononetin	945, 1246, 1248
	Formononetin 7-*O*-glucoside	1246
	Genistein	945, 1246, 1248
Trifolium lappaceum	Biochanin A	1246
	Formononetin	1246
	Formononetin 7-*O*-glucoside	1246
	Genistein	1246
Trifolium medium	Biochanin A	1252
	Daidzein	1252
	Formononetin	1252
	Formononetin 7-*O*-glucoside	1247
	Genistein	1247, 1252
Trifolium meduseum	Biochanin A	1248
	Formononetin	1248
	Genistein	1248
Trifolium ochroleucum	Biochanin A 7-*O*-glucoside	1250
Trifolium pannonicum	Biochanin A 7-*O*-glucoside	1250
Trifolium pauciflorum	Biochanin A	1246, 1248
	Formononetin	1246, 1248
	Formononetin 7-*O*-glucoside	1246
	Genistein	1246, 1248
Trifolium pilulare	Biochanin A	1246, 1248
	Formononetin	1246, 1248
	Formononetin 7-*O*-glucoside	1246
	Genistein	1246, 1248
Trifolium pratense	Biochanin A	940, 1167, 1246, 1253–1265
	Biochanin A 7-*O*-glucoside	1250, 1263, 1266–1268
	Biochanin A 7-*O*-glucoside 5-malonate (CCVI)	1263, 1267
	Daidzein	1167, 1168, 1258, 1263, 1264
	Daidzein 7-*O*-glucoside	1263
	Formononetin	940, 1013, 1167–1169, 1246, 1247, 1255, 1258–1260, 1262, 1263, 1265, 1269–1273
	Formononetin 7-*O*-glucoside	1246, 1247, 1250, 1263, 1266, 1268
	Formononetin 7-*O*-glucoside 6″-malonate (CLXVI)	1268
	Formononetin 7-*O*-glucoside 6″-methylmalonate (CLXVII)	1268
	Genistein	1050, 1167–1169, 1246, 1249, 1250, 1255, 1258, 1261, 1263, 1272
	Isoflavones	1274–1276
	Pratensein	1258, 1277–1279
Trifolium repens	Daidzein	1167, 1168
	Formononetin	1167, 1168, 1265, 1280
	Genistein	1050, 1167, 1168
	Isoflavones	1261
Trifolium sativum	Formononetin	1247
	Formononetin 7-*O*-glucoside	1247
Trifolium subterraneum	Biochanin A	934, 943, 945, 951, 1013, 1167, 1246, 1248, 1258, 1259, 1261, 1281–1288
	Biochanin A 7-*O*-glucoside	1250, 1268
	Biochanin A 7-*O*-glucoside 6″-malonate (CCVIII)	1268
	Biochanin A 7-*O*-glucoside 6″-methylmalonate (CCIX)	1268
	Daidzein	943, 1167, 1258, 1281–1283, 1285, 1286
	Formononetin	932, 934, 943, 945, 951, 1167, 1246, 1248, 1255, 1258, 1281–1287
	Formononetin 7-*O*-glucoside	1246, 1250, 1268
	Formononetin 7-*O*-glucoside 6″-malonate	1268
	Formononetin 7-*O*-glucoside 6″-methylmalonate	1268

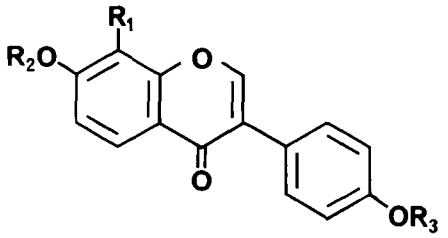
Table VII—*(Continued)*

Plant Name	Isoflavonoid	Reference
	Genistein	930, 932, 934, 943, 945, 951, 1013, 1167, 1246, 1248, 1249, 1255, 1258, 1259, 1261, 1281–1290
	Genistein 7-*O*-glucoside	1250
	Isoflavones	1274
Trifolium tembense	Biochanin A	1246
	Formononetin	1246
	Formononetin 7-*O*-glucoside	1246
Ulex bioivinii	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Ulex europaeus	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Ulex galli	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Ulex minor	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Ulex nanus	Genistein 7-*O*-glucoside	1065
Ulex parviflorus	Daidzein	1066
	Genistein	1066
	5-*O*-Methylgenistein	1066
Vigna sinensis	Isoflavones	1205
Wisteria brachybotrys	Afrormosin 7-*O*-glucoside	1291
Wisteria floribunda	Afrormosin 7-*O*-glucoside	1291
Wisteria sinensis	Isoflavones	1292
Moraceae		
Maclura pomifera	Osajin	1293, 1294
	Pomiferin (CCLXIX)	1294, 1295
Podocarpaceae		
Podocarpus spicatus	Genistein	1296
	Podospicatin (CCXLIV)	1296–1298
Rosaceae		
Prunus aequinoctalis	Genistein	1299
	Genistein 7-*O*-glucoside	1299
	Prunetin	1299
Prunus avium	Prunetin	1300
	Prunetin 4′-*O*-glucoside (CCI)	1064
Prunus emarginata	Prunetin	1300
	Prunetin 4′-*O*-glucoside	1064
Prunus mahaleb	Genistein	1301, 1302
	Prunetin	1301, 1302
Prunus maximowiczii	Genistein	1299
	Prunetin	1299
Prunus nipponica	Genistein	1299
	Genistein 7-*O*-glucoside	1299
	Prunetin	1299
Prunus puddum	Genistein	1303
	Padmakastein (CCLXXIX)	1304, 1305
	Padmakastin (CCLXXX)	1304
	Prunetin	1303, 1304
Prunus vericunda	Genistein	1308
	Prunetin	1308
Solanaceae		
Nicotiana tabacum	Isoflavonoids	1309



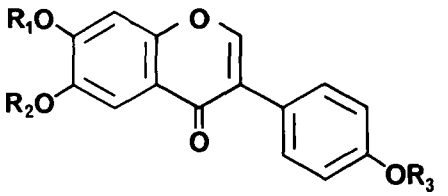
	R_1	R_2	R
CLXXV: 7,3′,4′-trihydroxyisoflavone	H	H	H
CLXXVI: 7,4′-dihydroxy-3′-methoxyisoflavone	H	CH_3	H
CLXXVII: calycosin	H	H	CH_3
CLXXVIII: calycosin 7-*O*-glucoside	Glu	H	CH_3
CLXXIX: calycosin 7-*O*-rhamnoglucoside	Rham·Glu	H	CH_3
CLXXX: pseudobaptigenin	H	—CH_2—	
CLXXXI: pseudobaptigenin 7-*O*-glucoside	Glu	—CH_2—	
CLXXXII: pseudobaptigenin 7-*O*-rhamnoglucoside	Rham·Glu	—CH_2—	
CLXXXIII: cladrin	H	CH_3	CH_3
CLXXXIV: cabreuvin	CH_3	CH_3	CH_3
CLXXXV: maxima substance B	—$CH_2CH{=}(CH_3)_2$	—CH_2—	

Structures of Isoflavonoids



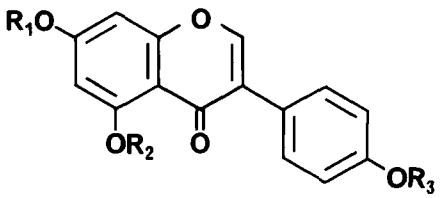
	R_1	R_2	R_3
CLIX: daidzein	H	H	H
CLX: daidzein 7-*O*-glucoside	H	Glu	H
CLXI: daidzein 7-*O*-rhamnoglucoside	H	Rham·Glu	H
CLXII: isoformononetin	H	CH_3	H
CLXIII: formononetin	H	H	CH_3
CLXIV: formononetin 7-*O*-glucoside	H	Glu	CH_3
CLXV: formononetin 7-*O*-rhamnoglucoside	H	Rham·Glu	CH_3
CLXVI: formononetin 7-*O*-glucoside-6″-malonate	H	Mal·Glu	CH_3
CLXVII: formononetin 7-*O*-glucoside-6″-methylmalonate	H	MeMal·Glu	CH_3
CLXVIII: di-*O*-methyldaidzein	H	CH_3	CH_3
CLXIX: durlettone	H	CH_3	$-CH_2CH=C(CH_3)_2$
CLXX: retusine	OH	H	CH_3
CLXXI: 8-*O*-methylretusine	OCH_3	H	CH_3
CLXXII: puerarin	Glu	H	H
CLXXIII: puerarin 4′,6″-diacetate	6-AcGlu	H	Ac
CLXXIV: puerarin xyloside	Glu	H or Xyl	Xyl or H

Structures of Isoflavonoids



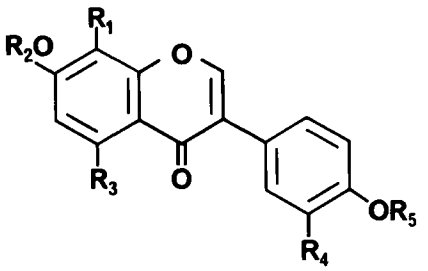
	R_1	R_2	R_3
CLXXXVI: 6,7,4′-trihydroxyisoflavone	H	H	H
CLXXXVII: glycitein	H	CH_3	H
CLXXXVIII: texasin	H	H	CH_3
CLXXXIX: texasin 7-*O*-glucoside	Glu	H	CH_3
CXC: afrormosin	H	CH_3	CH_3
CXCI: afrormosin 7-*O*-glucoside	Glu	CH_3	CH_3
CXCII: afrormosin 7-*O*-rhamnoglucoside	Rham·Glu	CH_3	CH_3

Structures of Isoflavonoids



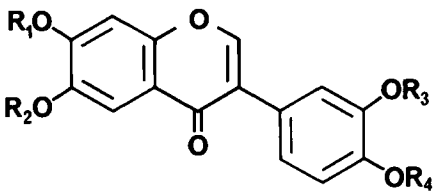
	R_1	R_2	R_3
CXCIII: genistein	H	H	H
CXCIV: genistein 4′-*O*-glucoside	H	H	Glu
CXCV: genistein 7-*O*-glucoside	Glu	H	H
CXCVI: genistein 7-*O*-neohesperiside	Neohesp	H	H
CXCVII: genistein 4′-*O*-rhamnoglucoside	H	H	Rham·Glu
CXCVIII: genistein 7-*O*-rhamnoglucoside	Rham·Glu	H	H
CXCIX: genistein 7-*O*-rutinoside	rutin	H	H
CC: prunetin	CH_3	H	H
CCI: prunetin 4′-*O*-glucoside	CH_3	H	Glu
CCII: 5-*O*-methylgenistein	H	CH_3	H
CCIII: biochanin A	H	H	CH_3
CCIV: biochanin A 7-*O*-glucoside	Glu	H	CH_3
CCV: biochanin A 7-*O*-rhamnoglucoside	Rham·Glu	H	CH_3
CCVI: biochanin A 7-*O*-glucoside 5-malonate	Glu	Mal	CH_3
CCVII: biochanin A 7-apiosylglucoside	Ap·Glu	H	CH_3
CCVIII: biochanin A 7-*O*-glucoside 6″-malonate	6-Mal·Glu	H	CH_3
CCIX: biochanin A 7-*O*-glucoside 6″-methylmalonate	6-MeMal·Glu	H	CH_3

Structures of Isoflavonoids



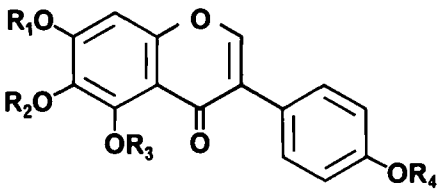
	R_1	R_2	R_3	R_4	R_5
CCX: orobol	H	H	OH	OH	H
CCXI: orobol 7-*O*-glucoside	H	Glu	OH	OH	H
CCXII: orobol 7-*O*-rhamnoglucoside	H	Rham·Glu	OH	OH	H
CCXIII: santal	H	CH_3	OH	OH	H
CCXIV: pratensein	H	H	OH	OH	CH_3
CCXV: maxima substance A	—OCH_2—		H	—CH_2O—	
CCXVI: derrustone	H	CH_3	OCH_3	—CH_2O—	
CCXVII: homotectoridin	OCH_3	Glu	OH	CH_3	H

Structures of Isoflavonoids



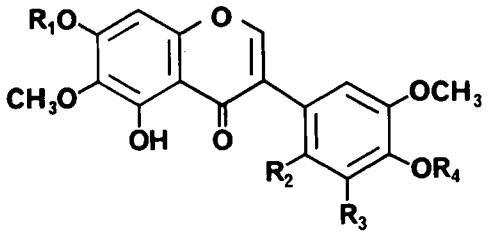
	R_1	R_2	R_3	R_4
CCXVIII: cladrastin	H	CH_3	CH_3	CH_3
CCXIX: 6,7,3′,4′-tetramethoxyisoflavone	CH_3	CH_3	CH_3	CH_3
CCXX: fujikinetin	H	CH_3	—CH_2—	
CCXXI: fujikinin	Glu	CH_3	—CH_2—	
CCXXII: 6,7-dimethoxy-3′,4′-methylenedioxyisoflavone	CH_3	CH_3	—CH_2—	

Structures of Isoflavonoids



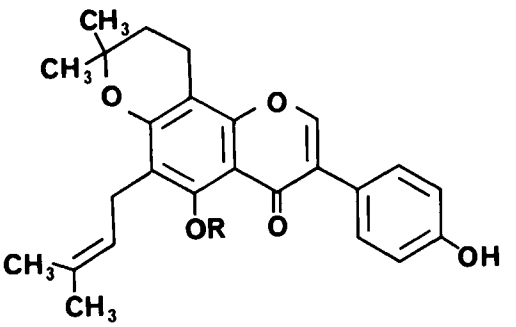
	R_1	R_2	R_3	R_4
CCXXIII: 6-hydroxygenistein	H	H	H	H
CCXXIV: 6-hydroxygenistein 7-*O*-rhamnoglucoside	Rham·Glu	H	H	H
CCXXV: tectorigenin	H	CH_3	H	H
CCXXVI: tectorigenin 7-*O*-glucoside	Glu	CH_3	H	H
CCXXVII: irilone	—CH_2—		H	H
CCXXVIII: irilone 4′-*O*-glucoside	—CH_2—		H	Glu
CCXXIX: irilone 4′-bioside	—CH_2—		H	Biose
CCXXX: irisolone	—CH_2—		CH_3	H
CCXXXI: 7-*O*-methyltectorigenin	CH_3	CH_3	H	H
CCXXXII: 7-*O*-methyltectorigenin 4′-*O*-rhamnoglucoside	CH_3	CH_3	H	Rham·Glu
CCXXXIII: muningin	CH_3	H	CH_3	H
CCXXXIV: 7,4′-dimethyltectorigenin	CH_3	CH_3	H	CH_3
CCXXXV: irisolidone	H	CH_3	H	CH_3

Structures of Isoflavonoids



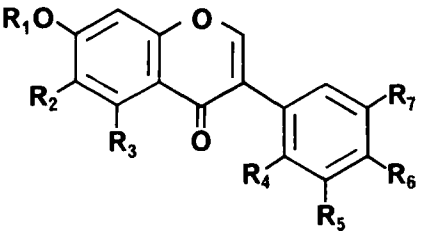
	R_1	R_2	R_3	R_4
CCXXXVI: iristectorigenin	H	H	H	H
CCXXXVII: caviunin	H	OCH_3	H	CH_3
CCXXXVIII: caviunin 7-*O*-glucoside	Glu	OCH_3	H	CH_3
CCXXXIX: irigenin	H	H	OH	CH_3
CCXL: irigenin 7-*O*-glucoside	Glu	H	OH	CH_3

Structures of Isoflavonoids



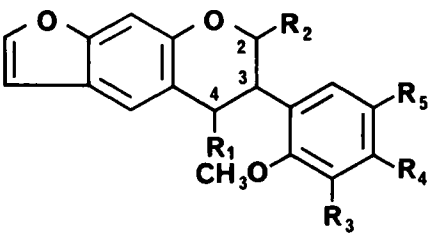
CCLXX: osajin, R = H
CCLXXI: 5-*O*-methylosajin, R = CH_3

Structures of Isoflavonoids



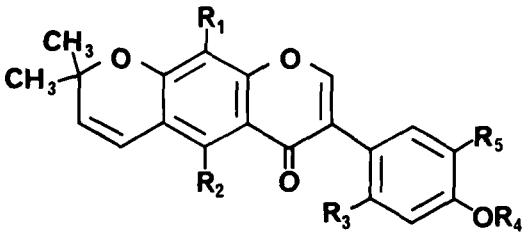
	R_1	R_2	R_3	R_4	R_5	R_6	R_7
CCXLI: 7,2′,4′-trihydroxyisoflavone	H	H	H	OH	H	H	H
CCXLII: dalpatein	H	OCH_3	H	OCH_3	H	—O—CH_2—O—	
CCXLIII: dalpatin	Glu	OCH_3	H	OCH_3	H	—O—CH_2—O—	
CCXLIV: milldurone	CH_3	OCH_3	H	OCH_3	H	—O—CH_2—O—	
CCXLV: podospicatin	H	OCH_3	OH	OH	H	H	OCH_3
CCXLVI: 6,7,3′-trimethoxy-4′5′-methylenedioxyisoflavone	CH_3	OCH_3	H	H	OCH_3	—O—CH_2—O—	
CCXLVII: 6,7,2′,4′,5′-pentamethoxyisoflavone	CH_3	OCH_3	H	OCH_3	OCH_3	OCH_3	H
CCXLVIII: tlatlancuayin	—CH_2—O—		OCH_3	OCH_3	H	H	H
CCXLIX: irisflorentin	—CH_2—O—		OCH_3	H	OCH_3	OCH_3	OCH_3
CCL: piscerythrone	H	H	OH	H	—CH_2CH=$C(CH_3)_2$	OH	OCH_3
CCLI: luteone	H	—CH_2CH=$C(CH_3)_2$	OH	OH	H	OH	H
CCLII: derrubone	H	—CH_2CH=$C(CH_3)_2$	OH	H	—O—CH_2—O—		H
CCLIII: maxima substance C	—CH_2CH=$C(CH_3)_2$	H	H	OCH_3	H	—O—CH_2—O—	

Structures of Isoflavonoids



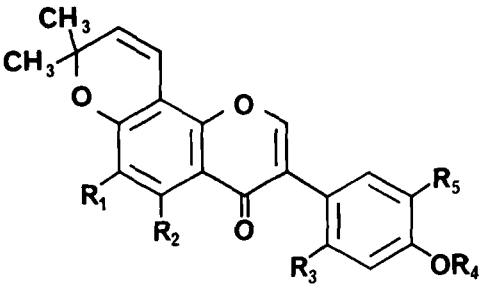
	R_1	R_2	R_3	R_4	R_5	other
CCLIV: nepseudin	=O	H_2	OCH_3	OCH_3	H	–
CCLV: neotenone	=O	H_2	H	—OCH_2O—		–
CCLVI: dehydroneotenone	=O	H	H	—OCH_2O—		$\Delta^{2,3}$
CCLVII: pachyrrizin	H	=O	H	—OCH_2O—		$\Delta^{3,4}$

Structures of Isoflavonoids



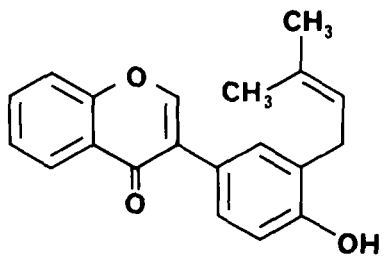
	R_1	R_2	R_3	R_4	R_5
CCLVIII: robustone	H	OH	H	—CH_2O—	
CCLIX: robustone methyl ether	H	OCH_3	H	—CH_2O—	
CCLX: scandenone	—CH_2CH=$C(CH_3)_2$	OH	H	H	H
CCLXI: auriculatin	—CH_2CH=$C(CH_3)_2$	OH	OH	H	H
CCLXII: auriculin	—CH_2CH=$C(CH_3)_2$	H	OH	CH_3	H

Structures of Isoflavonoids

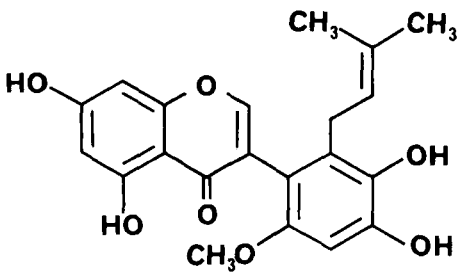


	R_1	R_2	R_3	R_4	R_5
CCLXIII: jamaicin	H	H	OCH_3	—CH_2O—	
CCLXIV: isoauriculatin	H	OH	OH	—CH_2CH=$C(CH_3)_2$	H
CCLXV: toxicarol isoflavone	H	OH	OCH_3	CH_3	CH_3
CCLXVI: durmillone	OCH_3	H	H	—CH_2O—	
CCLXVII: ichthynone	OCH_3	H	OCH_3	—CH_2O—	
CCLXVIII: scandinone	—CH_2CH=$C(CH_3)_2$	OCH_3	H	H	H
CCLXIX: pomiferin	—CH_2CH=$C(CH_3)_2$	OH	H	H	OH

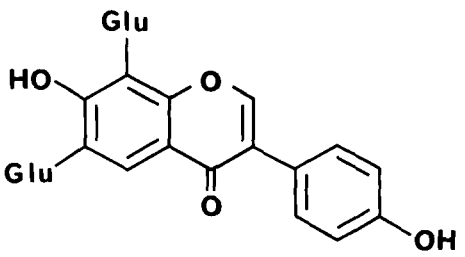
Structures of Isoflavonoids



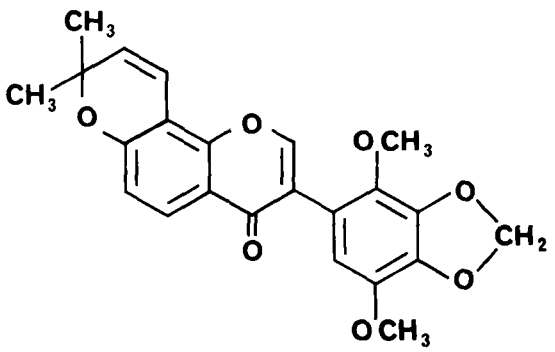
CCLXXII: chandalone



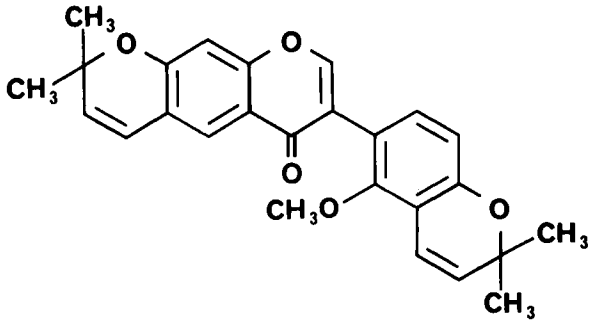
CCLXXIV: piscidone



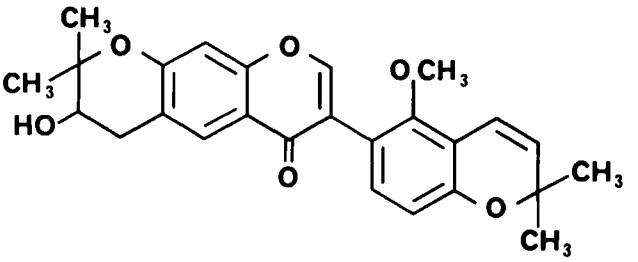
CCLXXIII: paniculatin



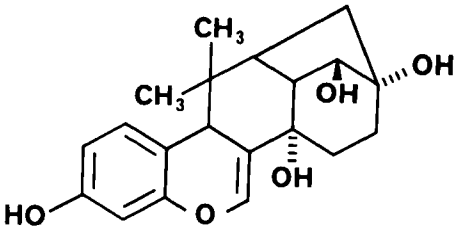
CCLXXV: ferrugone



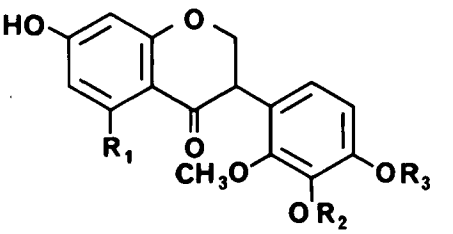
CCLXXVI: munetone



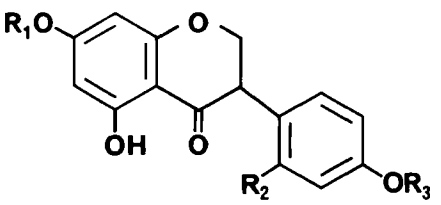
CCLXXVII: mundulone



CCLXXVIII: miroesterol

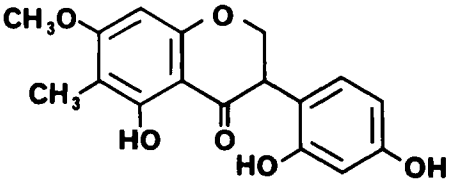


	R_1	R_2	R_3
CCLXXXV: violanone	H	H	CH_3
CCLXXXVI: 5,7,4′-trihydroxy-2′,3′-dimethoxyisoflavanone	OH	CH_3	H

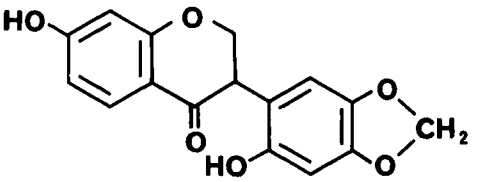


	R_1	R_2	R_3
CCLXXXIX: padmakistein	CH_3	H	H
CCLXXX: padmakistin	CH_3	H	Glu
CCLXXXI: 5,7-dihydroxy-4′-methoxyisoflavone	H	H	CH_3
CCLXXXII: dalbergioidin	H	OH	H
CCLXXXIII: ferreirin	H	OH	CH_3
CCLXXXIV: homoferreirin	H	OCH_3	CH_3

Structures of Isoflavonoids



CCLXXXVII: ougenin



CCLXXXVIII: sophorol

Structures of Isoflavonoids

Table VIII—Occurrence of Coumestans in Plants

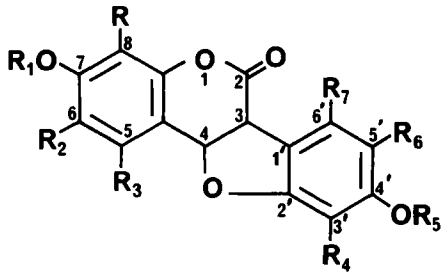
Plant Name	Coumestan	Reference
Compositae		
Eclipta alba	Wedelolactone (CCXCIX)	1310, 1311
	Demethylwedelolactone (CCXCVIII)	1311
Taraxacum officinale	Coumestrol	1312
Wedelia calendula	Wedelolactone	1313–1315
Gramineae		
Secale cereale	Coumestrol	1312
Leguminosae		
Cicer arietinum	Medicagol (CCC)	1316
	4′-*O*-Methylcoumestrol (CCXCI)	1316
Dalbergia decipularis	7,4′-Di-*O*-methylcoumestrol (CCXCIII)	1317
Glycine max	Coumestrol	1318, 1319
	Sojagol (CCCIII)	1318, 1319
Glycyrrhiza sp.	Isoglycyrol (CCCVII)	1320
	Glycyrol (CCCVI)	1320
	5-*O*-Methylglycyrol (CCCVIII)	1320
Maackia amurensis var. *buergeri*	Medicagol	1165
Medicago aculeata	Coumestrol	1321, 1322
Medicago arabica	Coumestrol	1321, 1322
Medicago arborea	Coumestrol	1321, 1322
Medicago blancheana	Coumestrol	1321, 1322

Table VIII—(*Continued*)

Plant Name	Coumestan	Reference
Medicago constricta	Coumestrol	1321
Medicago corulea	Coumestrol	1321, 1322
Medicago disciformis	Coumestrol	1321, 1322
Medicago dzhawakhetica	Coumestrol	1321, 1322
Medicago falcata	Coumestrol	1321, 1322
Medicago granadensis	Coumestrol	1321, 1322
Medicago hemicycla	Coumestrol	1321, 1322
Medicago hispida	Coumestrol	1323
Medicago intertexta	Coumestrol	1321, 1322
Medicago laciniata	Coumestrol	1321, 1322
Medicago littoralis	Coumestrol	1321, 1322, 1324, 1325
	4′-*O*-Methylcoumestrol	1325
	3′-Methoxycoumestrol (CCXC)	1325
Medicago minima	Coumestrol	1321, 1322
Medicago murex	Coumestrol	1321, 1322
Medicago orbicularis	Coumestrol	1321, 1322
Medicago polychroa	Coumestrol	1321, 1322
Medicago polymorpha	Coumestrol	1321, 1322
Medicago polymorpha var. *denticulata*	Coumestrol	1325
	4′-*O*-Methylcoumestrol	1325
	3′-Methoxycoumestrol	1325
Medicago praecox	Coumestrol	1321, 1322
Medicago rigidula	Coumestrol	1321, 1322
Medicago rotata	Coumestrol	1321, 1322
Medicago rugosa	Coumestrol	1321, 1322
Medicago sativa	Coumestrol	937, 942, 960, 1169, 1170, 1172, 1173, 1312, 1321–1323, 1326–1333
	5-Methoxy-4′-*O*-methylcoumestrol (CCXCII)	1170, 1334, 1335
	4′-*O*-Methylcoumestrol	1170, 1331, 1336
	Sativol (CCXCVI)	1170, 1331, 1337
	Medicagol	1170, 1331
	3′-Methoxycoumestrol	1331, 1338
	Trifoliol (CCXCVII)	1330, 1331
	Lucernol (CCXCIV)	1337
Medicago sauvagei	Coumestrol	1321, 1322
Medicago scutellata	Coumestrol	1321, 1322, 1325
	4′-*O*-Methylcoumestrol	1325
	3′-Methoxycoumestrol	1325
Medicago sogdiana	Coumestrol	1321, 1322
Medicago soleirolii	Coumestrol	1321, 1322
Medicago suffruticosa	Coumestrol	1321
Medicago tenoreana	Coumestrol	1321, 1322
Medicago tianshanica	Coumestrol	1321, 1322
Medicago tornata	Coumestrol	1321, 1322
Medicago truncatula	Coumestrol	1321, 1322, 1325
	4′-*O*-Methylcoumestrol	1325
	3′-Methoxycoumestrol	1325
Medicago turbinata	Coumestrol	1321, 1322
Medicago varia	Coumestrol	1321, 1322
Melilotus alba	Coumestrol	1322
Pachyrrhizus erosus	Erosnin (CCCIV)	1339, 1340
Phaseolus aureus	Coumestrol	1092, 1199, 1200, 1341
	Sojagol	1199
Psoralea corylifolia	Psoralidin (CCCV)	1342
Swartzia leiocalycina	6-Hydroxy-7-*O*-methylmedicagol (CCCI)	1343
	6-Hydroxy-5-methoxy-7-*O*-methylmedicagol (CCCII)	1343
Swartzia madagascariensis	7,4′-Di-*O*-methylcoumestrol	1344
Trifolium fragiferum	Coumestrol	960, 1323
Trifolium pratense	Coumestrol	1312, 1323, 1326, 1332
Trifolium repens	Coumestrol	960, 1280, 1312, 1323, 1326, 1345–1347
	4′-*O*-Methylcoumestrol	1346
	Trifoliol	1346, 1348
	Repensol (CCXCV)	1346
Trifolium subterraneum	Coumestrol	1281, 1282
Trifolium subterraneum var. *dwalganup*	Coumestrol	1323
Trigonella corniculata	Coumestrol	1322

this series is coumestrol (CCLXXXIX), and its isolation and estrogenic activity were first reported by Bickoff *et al.* (960). The coumestans are reported to have a higher order of estrogenic activity than the isoflavones (961). Table VIII gives a list of plants and their contained coumestans.

The synthetic stilbene derivative, diethylstilbestrol (CCCIX), is the prototype of the nonsteroidal estrogenic hormones. Of the natural stilbenes, rhaponticin (CCCX) is the only compound of this type reported to possess estrogenic activity. Knorr *et al.* (962) reported in 1956 that this compound could induce estrus in ovariectomized female rats. On the other hand, Klimek (963) reported in 1970 that rhaponticin produced only an insignificant increase in



		R	R_1	R_2	R_3	R_4	R_5	R_6	R_7
CCLXXXIX:	coumestrol	H	H	H	H	H	H	H	H
CCXC:	3′-methoxycoumestrol	H	H	H	H	OCH_3	H	H	H
CCXCI:	4′-*O*-methylcoumestrol	H	H	H	H	H	CH_3	H	H
CCXCII:	5-methoxy-4′-*O*-methylcoumestrol	H	H	H	H	H	CH_3	OCH_3	H
CCXCIII:	7,4′-di-*O*-methylcoumestrol	H	CH_3	H	H	H	CH_3	H	H
CCXCIV:	lucernol	H	H	OH	H	H	H	H	H
CCXCV:	repensol	H	H	H	H	H	H	H	OH
CCXCVI:	sativol	OH	CH_3	H	H	H	H	H	H
CCXCVII:	trifoliol	H	H	H	H	H	CH_3	H	OH
CCXCVIII:	demethylwedelolactone	H	H	H	OH	H	H	OH	H
CCXCIX:	wedelolactone	H	CH_3	H	OH	H	H	OH	H
CCC:	medicagol	H	H	H	H	H	$-CH_2-O-$		H
CCCI:	6-hydroxy-7-*O*-methylmedicagol	H	CH_3	OH	H	H	$-CH_2-O-$		H
CCCII:	6-hydroxy-5-methoxy-7-*O*-methylmedicagol	H	CH_3	OH	OCH_3	H	$-CH_2-O-$		H
CCCIII:	sojagol	H	H	H	H	$-CH_2CH_2-C(CH_3)_2-O-$		H	H
CCCIV:	erosnin	H	$-CH=CH-$		H	H	$-CH_2-O-$		H
CCCV:	psoralidin	H	H	$-CH_2-CH=C(CH_3)_2$	H	H	CH_3	H	H
CCCVI:	glycyrol	H	CH_3	$-CH_2-CH=C(CH_3)_2$	OH	H	H	H	H
CCCVII:	isoglycyrol	H	CH_3	$-CH_2CH_2-C(CH_3)_2-O-$	H		H	H	H
CCCVIII:	5-*O*-methylglycyrol	H	CH_3	$-CH_2-CH=C(CH_3)_2$	OCH_3	H	H	H	H

Structures of Coumestans

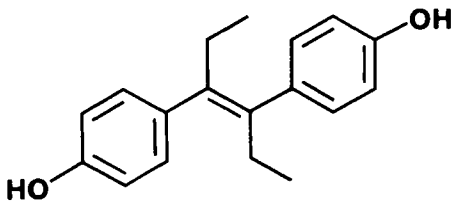
the uterine weight of immature mice. Therefore, the presence of estrogenic activity in this natural product remains to be demonstrated conclusively.

Another group of compounds has been reported to exhibit estrogenic activity. Wenzel and Rosenberg (964) reported that 6,4′-dihydroxyflavone (CCCXI) was estrogenic following subcutaneous injection, and Pretorius *et al.* (965) later found that quercetin (CXLVI) and robinin (CCCXII) showed slight estrogenic activity. Tricin (CCCXIII), from *Medicago sativa*, was also shown to have slight estrogenic activity (966). The estrogenic activity of quercetin has been questioned (967).

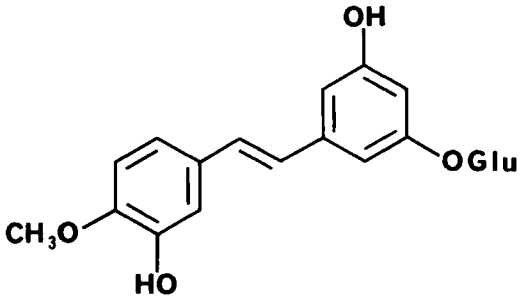
A number of reviews of plants containing estrogenic compounds have appeared (175, 928, 949, 968–1004).

A survey of 136 fodder plants for estrogenic activity appeared (1005) but was not available. Table IX presents a list of plants having estrogenic activity. A list of compounds obtained from plants that exhibit estrogenic activity is given in Table X.

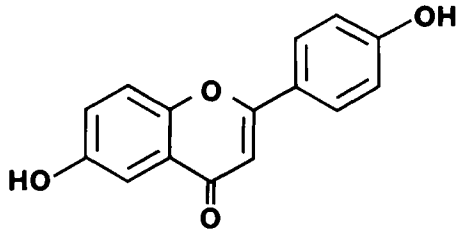
Humulus lupulus, *Avena sativa*, and *Oryza sativa* have been



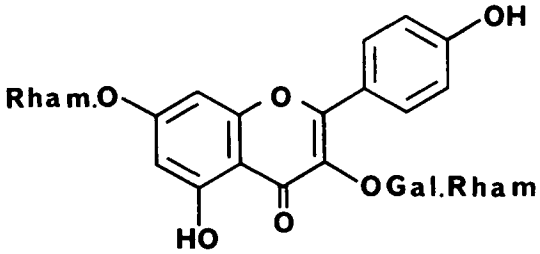
CCCIX: diethylstilbestrol



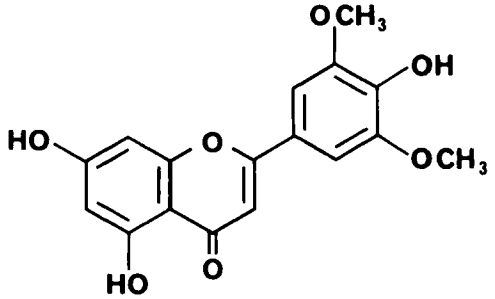
CCCX: rhaponticin



CCCXI: 6,4′-dihydroxyflavone



CCCXII: robinin



CCCXIII: tricin

shown to exhibit estrogenic properties (Table IX); these same plants have also been shown to induce ovulation (1006). Although there is no evidence of positive correlation between these two properties, it is of interest that the following plants also have been mentioned to induce ovulation: *Aralia cordata* (1006), *Citrus limon* (1006), *Lycium chinense* (1006, 1007), and *Raphanus sativus* (1006).

A number of plants have been reported from which products were obtained having properties similar to those of animal hormones. These products were not characterized, and no further details are available. Reviewers (928) have tended to assume that these products were estrogenic and have included them in tables of estrogenic plants. These claims may be unjustified and the plants are listed here rather than in Table IX, *i.e.*, *Convallaria majalis*,

Table IX—Plants Reported to Exhibit Estrogenic Activity

Plant Name		Reference
Agavaceae		
Agave americana		1349
Yucca aloifolia		1349
Anacardiaceae		
Mangifera indica		1350
Apocynaceae		
Funtumia sp.		1351
Holarrhena		1351
Araliaceae		
Panax ginseng		1352, 1353
Asclepiadaceae		
Asclepias tuberosa		263, 264, 1039
Balsaminaceae		
Impatiens balsamina		1354
Betulaceae		
Alnus glutinosa		968
Boraginaceae		
Lithospermum ruderale		177
Bromeliaceae		
Ananas comosus		194, 1355
Tillandsia aloifolia		1355
Tillandsia balbisiana		1355
Tillandsia circinata		1355
Tillandsia fasciculata		1355
Tillandsia juncea		1355
Tillandsia simulata		1355
Tillandsia tenuifolia		1355
Tillandsia usneoides		1356
Caprifoliaceae		
Sambucus niger		1357
Chenopodiaceae		
Beta vulgaris		924, 1358–1361
Compositae		
Calendula officinalis		1362
Carthamus tinctorius		1363
Chrysactinia mexicana		1364
Helianthus annuus		1365
Cruciferae		
Brassica napus		1365, 1366
Brassica pekinensis		1367
Cyperaceae		
Cyperus rotundus		1368
Euphorbiaceae		
Ricinus communis		1369
Gramineae		
Avena sativa		925, 968, 1038, 1370–1373
Agrostis tenuis		1374
Bromus mollis		1375–1378
Cynodon dactylon		1051
Dactylis glomerata	+	194, 1374, 1379–1384
	−	1382, 1383, 1385
Eragostris curvula		1386
Festuca pratensis		1371, 1374, 1387
Festuca rubra		1374, 1387
Festuca arundinacea		1383
Hordeum vulgare		1373, 1388
Hyparrhena filipendula		1051
Lolium perenne	+	194, 1374, 1379, 1380, 1383, 1389
	−	1383
Lolium rigidum	+	1390
	−	1391
Oryza sativa		1038, 1363, 1392
Phalaris arundinacea	+	1383
	−	1383
Phleum pratense	+	1374, 1381, 1384, 1393, 1394
	−	1374, 1379, 1395
Poa pratensis	+	1396
	−	1375, 1378, 1385, 1397
Poa trivialis		1374
Secale cereale	+	1385
	−	1385
Setaria ciliolata		1051
Triticum aestivum	+	1038, 1363, 1366, 1389, 1398–1400
	−	1375, 1378, 1385, 1397
Zea mays	+	1363, 1365, 1371, 1389, 1401

(continued)

Table IX—*(Continued)*

Plant Name		Reference
	−	1375, 1376, 1378
Labiatae		
Leonurus sibiricus		1402
Salvia officinalis		1403
Lauraceae		
Cinnamomum zeylanicum		1404
Leguminosae		
Arachis hypogaea		1363, 1365, 1405
Astragalus lentiginosus		1406
Astragalus miser		1407
Astragalus sinicus		1408
Butea superba		1223, 1409–1413
Butea sp.		1414–1417
Calopogonium muconoides		1405
Centrosema pubescens		1405
Ceratonia siliqua		1418
Cicer arietinum		1419
Crotalaria sp.		1405
Cytisus scoparius		1420
Glycine max	+	1365, 1375, 1389, 1405, 1408, 1421–1424
	−	1378
Glycyrrhiza glabra	+	1036, 1401, 1425–1433
	−	1434
Glycyrrhiza uralensis		1431
Glycyrrhiza sp.		1039
Leucaena glauca		1405
Lotus corniculatus	+	1383, 1389, 1396, 1435–1438
	−	1383
Lotus uliginosus		1439
Lupinus polyphyllus	+	1158
	−	1440
Lupinus termis		1441, 1442
Medicago falcata		1374
Medicago littoralis		1026, 1443
Medicago lupulina		1374, 1444
Medicago sativa		939, 1014, 1032, 1051, 1169, 1374–1377, 1381–1383, 1385, 1387, 1389, 1397, 1401, 1405, 1436, 1440, 1445–1478
Medicago tribuloides		1479
Medicago truncatula		1443
Melilotus officinalis		1473, 1475
Phaseolus aureus		1405
Phaseolus calcartus		1405
Phaseolus vulgaris		1040, 1480
Pisum sativum		1367, 1371, 1458, 1473, 1475
Pueraria javanica		1405
Trifolium alexandrium	+	1373, 1429, 1481, 1482
	−	1372
Trifolium fragiferum	+	1483
	−	1484
Trifolium hybridum		1374, 1383
Trifolium incarnatum		1374, 1444
Trifolium pratense	+	959, 975, 1000, 1011, 1013, 1032, 1034, 1169, 1258, 1260, 1367, 1371, 1374, 1379, 1381, 1383, 1384, 1387, 1389, 1393, 1394, 1397, 1401, 1436, 1437, 1439, 1444, 1445, 1450, 1467, 1471, 1473, 1475, 1476, 1485–1514
	−	1484
Trifolium repens	+	1290, 1345, 1374, 1376, 1383, 1389, 1395, 1396, 1411, 1412, 1435–1437, 1440, 1459, 1471, 1475, 1476, 1483, 1515–1521
	−	1383, 1397, 1473, 1483, 1484, 1510, 1511, 1522, 1523
Trifolium subterraneum		930, 931, 935, 936, 975, 1000, 1010, 1012, 1013, 1259, 1281, 1287, 1371, 1384, 1390, 1444, 1463, 1479, 1483, 1492, 1514, 1515, 1524–1549
Vicia americana		1407
Vicia angustifolia		1475
Vigna sesquipedalia		1405
Vigna sinensis		1405
Liliaceae		
Allium porrum		1349
Allium ursinum		1550
Chamaelirium luteum		1039
Phalangium liliago		1349
Tulipa gesneriana		1551, 1552
Veratrum californicum		153
Linaceae		
Linum usitatissimum		1363, 1365, 1389
Malvaceae		
Althaea rosea		1354
Meliaceae		
Melia azadirachta		1553
Moraceae		
Artocarpus integrifolia		1350
Ficus infectoria		1350
Ficus religiosa		1350
Humulus lupulus	+	962, 1353, 1367, 1554–1559
	−	1560
Morus sp.		1350
Moringaceae		
Moringa oleifera		1405
Myrtaceae		
Eucalyptus sp.		1561
Eugenia jambolana		1350
Nymphaeaceae		
Nuphar luteum		1354, 1562
Oleaceae		
Olea europaea		1363, 1365
Palmae		
Cocos nucifera		1363
Elaeis guineensis		925, 1365
Phoenix dactylifera		1043
Serenoa repens		1563
Pinaceae		
Pinus ponderosa	+	1564
	−	1565, 1566
Polygonaceae		
Rheum rhaponticum		968
Punicaceae		
Punica granatum		1567
Rosaceae		
Prunus cerasus		924
Prunus domestica		924
Rubiaceae		
Coffea arabica		1568
Ophiorrhiza mungos		1405
Salicaceae		
Salix babylonica		1349
Salix caprea		926, 968, 1354, 1366, 1388, 1562, 1569
Solanaceae		
Lycium chinense		1570
Solanum tuberosum		924, 1366
Sterculiaceae		
Theobroma cacao		1365
Tiliaceae		
Tilia cordata		1349
Tilia europaea		1357
Tilia platyflora		1349
Umbelliferae		
Daucus carota		1399, 1400, 1571
Foeniculum vulgare		1561
Heracleum sosnowskyi		1401
Levisticum officinale		1572
Petroselinum crispum		924
Pimpinella anisum		1428, 1429, 1561
Urticaceae		
Musanga cecropioides		1573
Urtica sp.		1357
Violaceae		
Viola odorata		1574
Zingiberaceae		
Costus speciosus		1575
Unidentified grasses		1371, 1447, 1547, 1576–1580

Table X—Compounds Reported to Have Estrogenic Activity

Compound Name		Reference
Anethole (CCCXIV)		1561
Anisole (CCCXV)		1561
Asiaticoside (CCCXVI)		1172
Biochanin A (CCIII)		999, 1011, 1031–1034, 1246, 1259, 1581
Cafesterol (CCCXVII)	+	1582, 1583
	−	1584–1587
Clupanodonic acid		1588
Colchicine (CXVIII)		1589
Coumestrol (CCLXXXIX)		994, 999, 1011, 1014, 1590–1598
Daidzein (CLIX)	+	1031–1034
	−	928
Deserpidine (CCCXVIII)		1599
Diosgenin (CCCXIX)		1600
17α-Estradiol (CLV)		1601
Estriol (CLVII)		1601
Estrone (CLVIII)		1601
Formononetin (CLXIII)	+	999, 1011, 1014, 1031–1034, 1259, 1273
	−	928, 972, 1034
Genistein (CXCIII)		930, 933, 999, 1011, 1014, 1031–1034, 1259, 1592, 1596, 1602–1604
Genistein 7-*O*-glucoside (CXCV)		1375, 1478, 1591
Genistein 4′-*O*-glucoside (CXCIV)		1605
Gibberellic acid (CCCXX)		1606, 1607
Miroestrol (CCLXXVIII)		994, 1608–1611
Nicotine (X)	+	1613–1615
	−	1616
Phloretin (CCCXXI)		1617
Pilocarpine (CXXVI)		1618
Podocarpic acid (CCCXXII)		1619
Prunetin (CC)		928
Reserpine (LXXXIX)	+	1620–1624
	−	1620–1629
Rhaponticin (CCCX)	+	962
	−	963
β-Sitosterol (CXLII)		1035, 1037
Glycyrrhiza glabra steroids		1427

Table XI—Relative Potency of Sterol Estrogens, Coumestrols, and Isoflavones

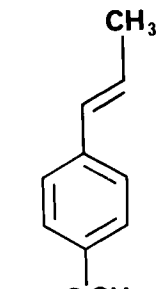
Compound	Quantity Required to Produce a 25-mg Uterus, μg	Relative Potency
Control	—	—
Diethylstilbestrol	0.083	100,000
Estrone	1.20	6,900
Coumestrol	240	35
Genistein	8,000	1.00
Daidzein	11,000	0.75
Biochanin A	18,000	0.46
Formononetin	32,000	0.26

Malus pumila, Petroselinum crispum, Prunus cerasus, Rheum rhaponticum, and *Solanum tuberosum* (1008).

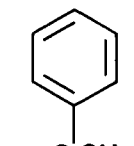
The metabolism of phytoestrogens in animals has been investigated in the sheep (1004–1014), rat (1015), cow (1016, 1017), fowl (1018–1021), other animals (1022), and liver enzyme systems (1023), and the effect of phytoestrogens on the blood in sheep has been studied (1024–1027).

If one inspects the structures of the estrogenic sterols (CXLII and CLV–CLVIII), isoflavones (CLIX–CCLXXXVIII), and coumestans (CCLXXXIX–CCCVIII), one can see a striking similarity of the skeletal structures of these compounds with the structure of the synthetic estrogen diethylstilbestrol (CCCIX).

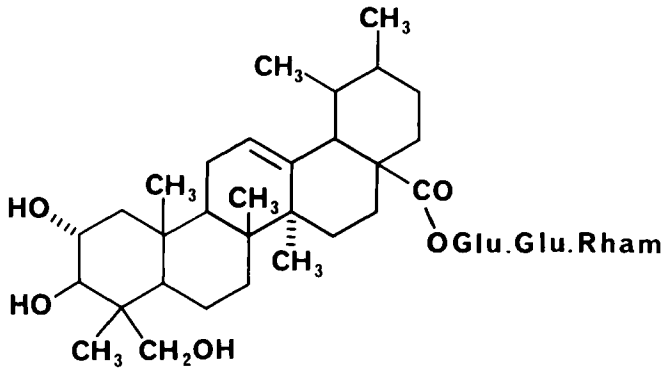
Recently, coumestrol (CCLXXXIX) and genistein (CXCIII) were shown to compete with 17β-estradiol (CLVI) for binding sites on a macromolecular component of the uterus from 6-day pregnant rabbits. The binding affinity of these compounds was related to their reported estrogenic potency; *i.e.*, one part by weight of 17β-estradiol, 70 of coumestrol, and 175 of genistein produced equivalent inhibition of the uptake *in vitro* of ^{3}H-17β-estradiol by the uterine receptor. Biochanin A (CCIII), formononetin (CLXIII), 4′-*O*-methylcoumestrol (CCXCI), sativol (CCXCVI), and medicagol (CCC) did not significantly inhibit 17β-estradiol binding, suggesting that free hydroxyl groups in positions 7 and 12



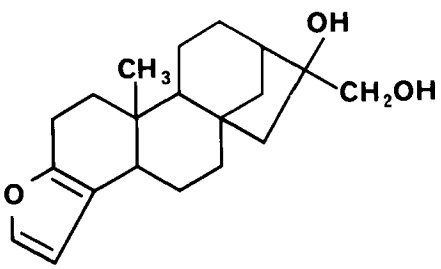
CCCXIV: anethole



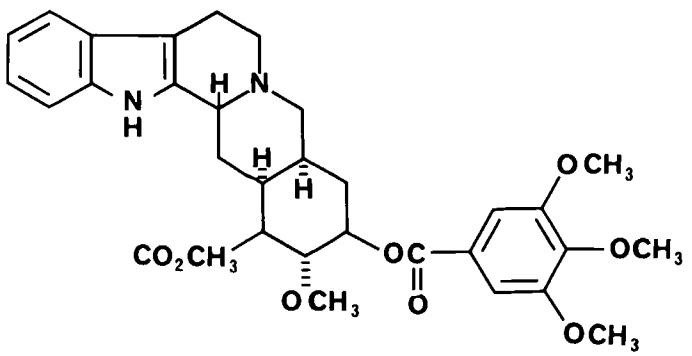
CCCXV: anisole



CCCXVI: asiaticoside

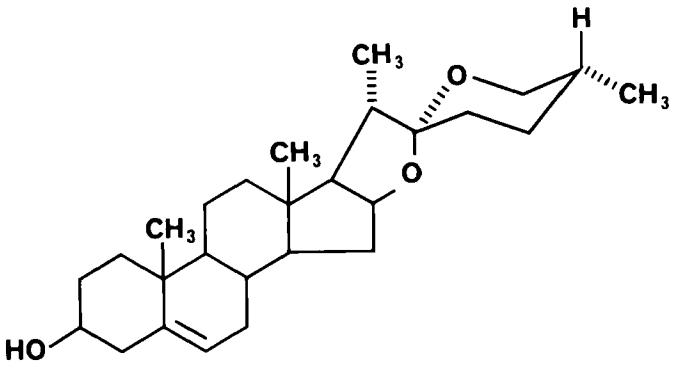


CCCXVII: cafesterol

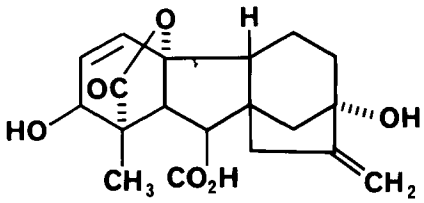


CCCXVIII: deserpidine

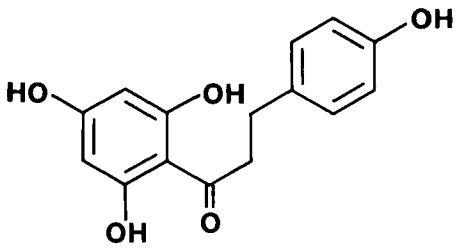
Structures of Additional Compounds Having Estrogenic Activity



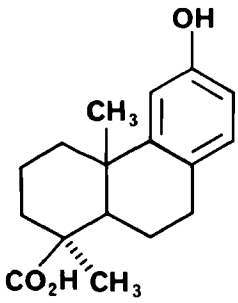
CCCXIX: diosgenin



CCCXX: gibberellic acid

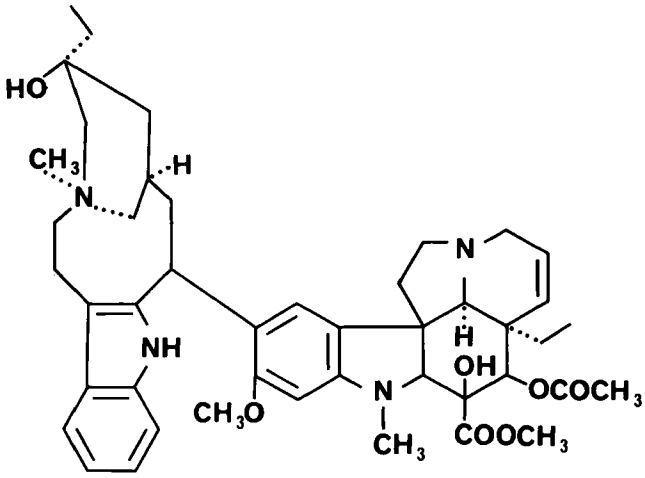


CCCXXI: phloretin

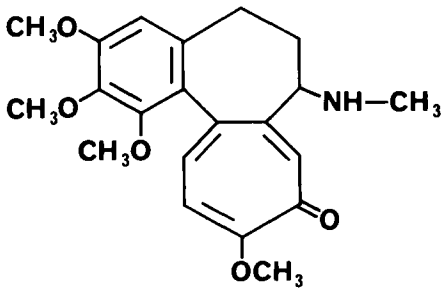


CCCXXII: podocarpic acid

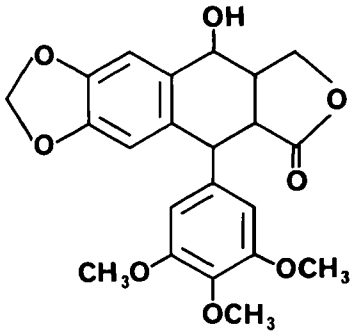
Structures of Additional Compounds Having Estrogenic Activity



CCCXXIII: vinblastine



CCCXXIV: demecolcine



CCCXXV: podophyllotoxin

of coumestans and isoflavones are essential for effective interaction with the estrogen receptor. The 7- and 4′-methoxycoumestans and isoflavones tested appeared to be proestrogens, able to bind to the uterine receptor only after *O*-demethylation *in vivo* (1029).

The order or degree of the biological activity of each of the three main groups of natural estrogens has been investigated (1030). The sterol estrogens were found to be of the highest order of activity, followed by the coumestrols and then the isoflavones. The relative potency of each substance, tested by the mouse-uterine weight bioassay method, with genistein arbitrarily chosen as the reference substance, is given in Table XI.

Other investigators studied the relative estrogenicity of the isoflavones and coumestan-type compounds. Comparison of the estrogenic activity of prunetin (CC), genistein (CXCIII), daidzein (CLIX), biochanin A (CCIII), and formononetin (CLXIII) led to the conclusion that the 5-hydroxyl group was essential for estrogenic activity (928). Genistein, biochanin A, and prunetin were estrogenic, while daidzein and formononetin were devoid of activity. Coumestrol (CCLXXXIX) was found to be many times more active than any of the isoflavonoid derivatives when administered intrarumenally to ovariectomized animals (1011). More recently, Leavitt and Meismer (999) reported that the relative estrogenic properties were in the order coumestrol > genistein > biochanin A > formononetin.

In addition to the work mentioned previously, some studies (1031–1034) have shown that daidzein was the most active isoflavonoid derivative in the mouse-uterine weight assay; biochanin A and genistein were of lesser but approximately equal activity, and

formononetin was essentially inactive. The other isoflavones listed in Table VII have not yet been examined for estrogenic activity, but they have been included because of potential estrogenic activity.

CYTOTOXIC AGENTS AS ANTIFERTILITY DRUGS

Certain naturally occurring cytotoxic agents have been shown to elicit an antifertility effect in laboratory animals, either by local or systemic routes of administration (70, 1630, 1631). For such a compound to be useful as an antifertility agent, it would have to be completely nontoxic, without teratogenic manifestation in marginal doses, and 100% effective (70). A number of plant products have been shown to elicit varying degrees of antifertility activity due to cytotoxicity. For example, vinblastine (CCCXXIII) from *Catharanthus roseus* (Apocynaceae), when administered to rabbits, reduced the percentage of normal fetuses at term to 0–33.3%; however, there were three fetal abnormalities produced in a group of 60 rabbits (70). An attempt was made to prevent this toxic effect by the concomitant administration of glutamic acid, which is known to prevent general toxic effects of vinblastine in mice. When administered prior to vinblastine, a 53.6% implantation rate was observed, with only 41.2% developing into normal fetuses (70).

Demecolcine (CCCXXIV), derived from several *Colchicum* species (Liliaceae), appears to act directly on the fetus and not on the placenta. This alkaloid, in doses of 2–8 mg/kg sc, destroyed the fetuses of rabbits 13–16 days pregnant. The drug was less effective when given orally (70). One or two doses of 2.5 mg/kg ip of demecolcine given to pregnant rats destroyed all litters when given between Days 11 and 19 of gestation. Fetuses showed marked edema, ascites, and hemorrhagic staining of internal organs and skin 6–12 hr after administration of the drug. No gross abnormalities were seen, but stunting was observed in a few surviving fetuses of rats treated with lower doses (70).

Podophyllotoxin (CCCXXV), a lignan derived from *Podophyllum* species (Berberidaceae), was administered to mice as a single subcutaneous dose of 0.25 mg, either immediately after detection of a vaginal plug or 3, 6, 12, or 14 days thereafter. Pregnancy did not continue in animals treated 3 days or more after copulation. Administered within 24 hr after copulation, podophyllotoxin was only occasionally effective (1631).

A number of plants listed in Tables II and III have a folkloric reputation as antifertility agents or have shown some degree of antifertility activity in laboratory animals. Table XII gives the names of those plants found in Tables II and III that are known to contain cytotoxic compounds, or crude extracts of which have shown cytotoxic or antitumor activity and thus could owe their antifertility activity to this mechanism. Known cytotoxic agents are also indicated for each plant in Table XII.

DISCUSSION

It can be seen in Table III that the effects, or lack thereof, of various plant extracts on the fertility of laboratory animals has been expressed in a number of ways by different workers. In the light of current knowledge concerning the reproductive cycles of the various laboratory species *(vide supra)*, it sometimes has not been clear from the procedures and data reported by some workers as to how they arrived at their conclusions that a particular mechanism was responsible for the antifertility effect produced by a given extract. Furthermore, lack of the use of control (vehicle-treated) animals in many studies leaves one to guess what would have been the expected rate of successful pregnancies in the strains and species used had no plant extract been administered. However, a clue was offered by Khanna *et al.* (103); in their estimation, an extract showing 100% "inhibition of implantation" had significant activity, one showing at least 50% inhibition had encouraging activity, and one showing less than 50% inhibition had no significant activity.

With such criteria in mind, it can be seen that some plants listed in Table III do not appear to have antifertility activity in spite of the fact that many of these same plants have a folkloric reputation for having contraceptive activity (Table II). If the fact that species variability *(vide supra)* could be at least partly responsible for the lack of correlation is ignored, it may be considered possible that such a lack could be due at least partly to the testing procedures used. For example, as indicated in the footnote to Table II, a number of plants (including *Calotropis gigantea, Carica papaya, Momordica charantia, Dendrocalamus strictus, Uraria lagopoides, Gloriosa superba, Piper longum,* and *Apium graveolens*) have been stated to have antifertility effects although it is possible that their activity might more narrowly fall into the abortifacient or emmenagogic categories. The plants just named, however, when tested in animals, were never administered past the 7th day of pregnancy; that is, they were administered until just barely beyond the time of implantation, probably not long enough to test for any abortifacient effect other than a very early acting one.

A few of the plants listed in Table II as having a folkloric reputation as antifertility agents are reported in Table III as having antiovulatory activity; these plants are *Apocynum androsaemifolium, Asclepias hallii,* and *Hibiscus rosa-sinensis. Semecarpus anacardium, Mallotus philippinensis, Ricinus communis, Abrus precatorius,* and *Plumbago zeylanica* also are listed in both Tables II and III. These plants, however, apparently have not been tested for antiovulatory activity. As indicated in Table III, extracts of these plants have been administered to animals following mating and have been shown to be ineffective in inhibiting pregnancy under these conditions, probably due to a lack of interceptive activity and/or anti-implantational activity *per se (vide supra)*. That these plants do not possess antifertility activity by means of an antiovulatory effect has not been shown.

Scheme I suggests a means by which one may test for the various possible mechanisms of antifertility activity in the female mammal. If one merely wishes to determine whether a given extract has contraceptive, interceptive, and/or abortifacient activity, the entire procedure can be carried straight through. If activity is demonstrated early in the scheme, obviously additional animals will be required to examine for later effects. As indicated earlier in this paper, a given compound may inhibit fertility by more than one mechanism and/or at more than one site. The offshoots at the right of the scheme indicate the means by which further details concerning mechanism(s) of action may be elucidated. The rat, which appears to be the most commonly used test species, is the species indicated in Scheme I; other species, of course, have been and can be used, but variations among their reproductive cycles (Table I and Ref. 4) should be considered.

It appears, then, that investigators interested in the further

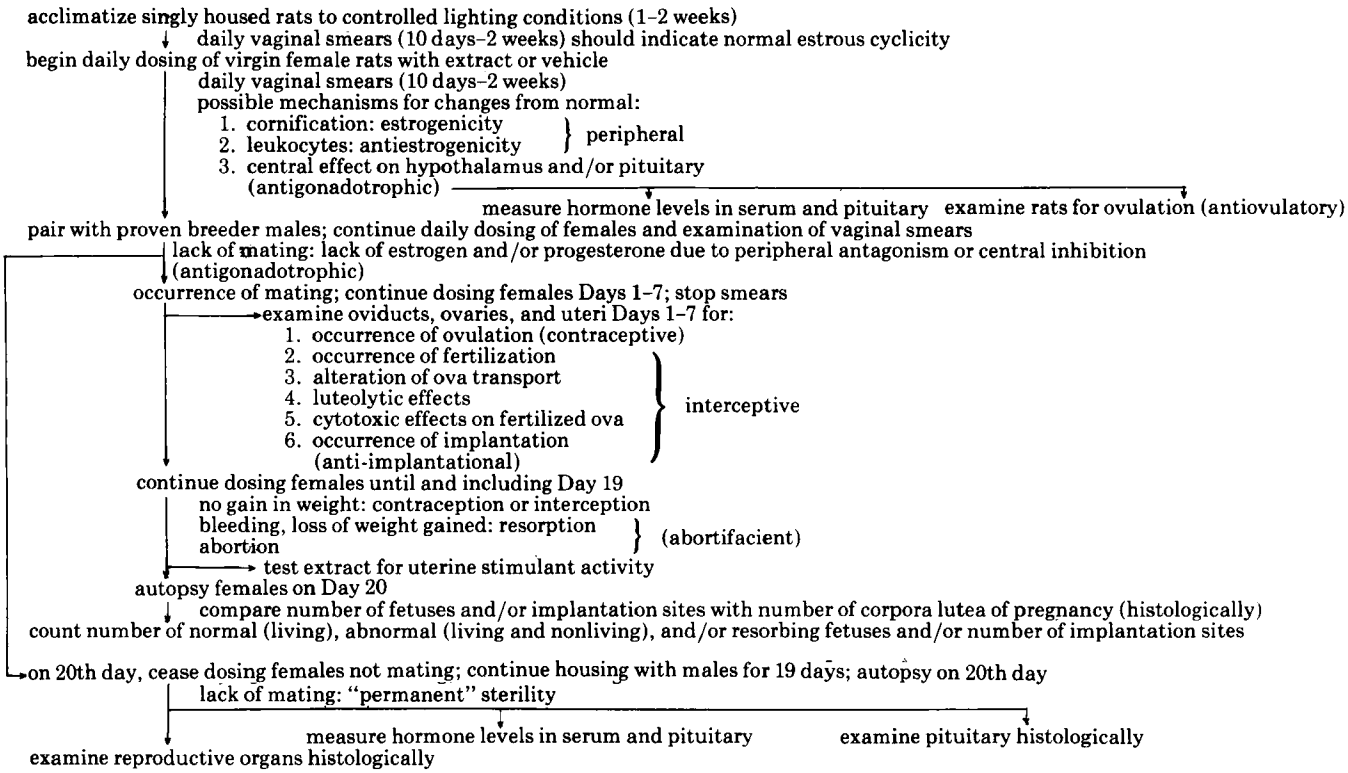
Table XII—Plants Whose Alleged or Demonstrated Antifertility Activity Could Be Explained on the Basis of Cytotoxicity

Plant Name	Cytotoxic Agent	Reference
Annonaceae		
Annona squamosa	Cytotoxicity	1640
Apocynaceae		
Apocynum androsaemifolium	Cardenolides	1632, 1633
Apocynum cannabinum	Apocannoside	1634, 1635
Catharanthus roseus	Vinblastine, vincristine, leurosine, leurosivine, rovidine, leurosidine	1636
Cerbera manghas	Cardenolides	1632
Nerium indicum	Cardenolides	1632
Rauvolfia serpentina	Reserpine	1671
Thevetia peruviana	Cardenolides	1632

(continued)

Table XII—(*Continued*)

Plant Name	Cytotoxic Agent	Reference
Aristolochiaceae		
Aristolochia clematitis	Aristolochic acid	1632, 1637
Aristolochia indica	Aristolochic acid	1632, 1637
Asarum canadense	Aristolochic acid	1632, 1635, 1637, 1638
Asclepiadaceae		
Asclepias hallii	Cardenolides	1632
Asclepias syriaca	Cardenolides	1632
Marsdenia cundurango	Cytotoxicity	1639
Berberidaceae		
Podophyllum peltatum	Podophyllotoxins	1632, 1641, 1642
Boraginaceae		
Lithospermum arvense	Cytotoxicity	1635
Symphytum officinale	Cytotoxicity	1643, 1644
Compositae		
Artemisia sp.	Sesquiterpene lactones	1632
Cruciferae		
Capsella bursa-pastoris	Cytotoxicity	1633
Raphanus sativus	Cytotoxicity	1645
Cucurbitaceae		
Citrullus colocynthis	Cucurbitacins	1632, 1646–1648
Cucumis sativus	Cytotoxicity	1649
Ecballium elaterium	Cucurbitacins	1632, 1646, 1647, 1650
Luffa cylindrica	Cucurbitacins	1632, 1646, 1648
Momordica charantia	Cucurbitacins	1639
Momordica tuberosa	Cucurbitacins	1632
Ericaceae		
Arctostaphylos uva-ursi	Cytotoxicity	1667
Euphorbiaceae		
Euphorbia resinifera	Cytotoxicity	1646
Excoecaria agallocha	Cytotoxicity	1651
Jatropha curcas	Jatrophone	1662
Mallotus philippinensis	Cytotoxicity	1652
Stillingia sylvatica	Cytotoxicity	1635
Leguminosae		
Abrus precatorius	Abrin	1653
Gleditsia horrida	Cytotoxicity	1654
Phaseolus aureus	Cytotoxicity	1640
Pisum sativum	Cytotoxicity	1655
Psoralea corylifolia	Cytotoxicity	1654
Liliaceae		
Asparagus officinalis	Cytotoxicity	1633
Colchicum autumnale	Colchicine, demecolcine	1656–1658
Loranthaceae		
Phoradendron flavescens	Cytotoxicity	1649, 1659, 1660
Lythraceae		
Lawsonia inermis	Lawsone	1651
Malvaceae		
Gossypium herbaceum	Gossypol	1659, 1661
Menispermaceae		
Cissampelos pareira	Cytotoxicity	1663
Stephania hernandifolia	Cytotoxicity	1656, 1664
Myristicaceae		
Myristica fragrans	Cytotoxicity	1654
Papaveraceae		
Chelidonium majus	Protopine	1665
Polygonaceae		
Polygonum multiflorum	Cytotoxicity	1654
Polypodiaceae		
Dryopteris filix-mas	Cytotoxicity	1652
Punicaceae		
Punica granatum	Cytotoxicity	1654
Ranunculaceae		
Aconitum napellus	Cytotoxicity	1639
Paeonia sp.	Cytotoxicity	1654, 1666, 1667
Rosaceae		
Sanguisorba officinalis	Cytotoxicity	1654
Rutaceae		
Citrus aurantium	Cytotoxicity	1654
Evodia rutaecarpa	Cytotoxicity	1660
Santalaceae		
Santalum album	Cytotoxicity	1654
Saxifragaceae		
Hydrangea arborescens	Cytotoxicity	1633
Scrophulariaceae		
Digitalis lanata	Cardenolides	1632
Rehmannia glutinosa	Cytotoxicity	1654
Simaroubaceae		
Simarouba amara	Cytotoxicity	1652
Solanaceae		
Solanum dulcamara	β-Solamarine	1669
Umbelliferae		
Siler divaricatum	Cytotoxicity	1654



Scheme I

study of plants as a source of new antifertility agents should note certain data that have been presented herein. First, a proper dosing schedule (Scheme I) should be followed in the testing that will allow the investigator to detect plants, the activity of which may be caused by constituents having a mechanism of interest. Second, it is apparent from published data that many studies have lacked adequate controls; vehicle-treated animals should always be studied concurrently so that the investigator can know the normal pregnancy rate for that particular strain and species of animal. Third, one should not rely on a single solvent extract for testing. For example, it has been shown in the case of *Medicago sativa* that the ether extract was estrogenic, that the chloroform extract was antiestrogenic, and that the acid–water extract interfered with seminal vesicle growth (141). In the case of *Ocimum sanctum*, the benzene extract showed 80% antifertility activity, the petroleum ether extract 60%, and the ethanol extract less than 50% (99).

To separate plant material for testing into fractions of differing polarity, it seems that each plant should be extracted first with petroleum ether. The marc should then be extracted with either ethanol or methanol, with this extract being partitioned between chloroform and water. The resulting three extracts, *i.e.*, petroleum ether, chloroform, and water, should then each be evaluated for antifertility effects; one should not rely on an evaluation of a single solvent extract alone.

Finally, the plant names presented in Tables II and III have been examined and compared with the data presented in Tables IV–XII. From this comparison, we have deleted all plant names in Tables II and III that have also been found in Tables IV–XII. This new list of suggested plants to investigate for antifertility activity is presented in Table XIII.

Table XIII—Plants Suggested to Be Reinvestigated for Antifertility Activity

Plant Name	Plant Part[a]	Reference
Aizoaceae		
Trianthema pentandra	—	192
Trianthema portulacastrum	—	192
Amaranthaceae		
Achyranthes aspera	—	192
Amaranthus retroflexus	PL	169
Amaranthus spinosus	—	171
Amaryllidaceae		
Stenomesson variegatum	—	92
Anacardiaceae		
Rhus trilobata	LF	92
Semecarpus anacardium	RT, SD	90, 103, 192
Semecarpus stellata	RT	92
Annonaceae		
Artabotrys odoratissimus	LF	104
Araceae		
Acorus calamus	RT	91
Anthurium tessmannii	IF	92, 93
Arisaema atrorubens	RZ	92
Ariasaema triphyllum	RT	90, 92
Philodendron dyscarpium	IF	92, 93

(continued)

Table XIII—(*Continued*)

Plant Name	Plant Part[a]	Reference
Urospatha antisylleptica	SP	92, 93
Araliaceae		
Fatsia horrida	PL	169
Hedera helix	FR, FL	90, 92
Asclepiadaceae		
Marsdenia cundurango	BK	171
Basellaceae		
Basella alba	RT	91
Berberidaceae		
Epimedium alpinum	LF, RT	90
Betulaceae		
Betula bhojpattra	SB	91
Bignoniaceae		
Dolichandrone falcata	—	192
Boraginaceae		
Anchusa officinalis	PL	170
Borago officinalis	PL	169
Cordia dichotoma	FR	91
Cordia quarensis	RT	90
Echium vulgare	PL	170
Lithospermum arvense	PX, PL	90, 169
Lithospermum croceum	PX, RT	169
Lithospermum distichum	PX, RT	169
Lithospermum latifolium	PX, RT	169
Lithospermum officinale	PX, RT, LF, PL	92, 114, 169, 188
Lithospermum ruderale	PX, RT	90, 92, 97, 111, 112, 169, 180, 188
Symphytum officinale	PL, RT	115
Bromeliaceae		
Tillandsia decomposita	FS	92
Buddlejaceae		
Buddleja asiatica	—	192
Capparidaceae		
Crataeva nurvala	SB	91, 92
Caprifoliaceae		
Lonicera ciliosa	LF	92, 117
Caryophyllaceae		
Dianthus superbus	PL	120, 121
Vaccaria pyramidata	PL	121
Celastraceae		
Celastrus paniculatus	—	192
Chenopodiaceae		
Chenopodium album	LF	127
	PL	90, 169
Combretaceae		
Terminalia catappa	—	171
Commelinaceae		
Aneilema scapiflorum	—	171
Compositae		
Achillea millefolium	PL	90
Ambrosia artemisifolia	PL	169
Artemisia maritima	—	171
Atractylis gummifera	RT	92
Chrysanthemum indicum	—	171, 192
Cnicus benedictus	PL	90, 169
Echinops echinatus	—	171
Eupatorium odoratum	RT	90
Franseria artemisioides	PL	92
Solidago odora	LF	171
Tanacetum umbelliferum	—	171, 192
Convolvulaceae		
Cuscuta reflexa	—	171, 192
Crassulaceae		
Crassula abyssinica	PL	98
Cruciferae		
Anastatica hierochuntica	—	171, 192
Brassica campestris	—	171
Brassica nigra	SD	91, 171
Isatis oblongata	PL	121
Lepidium sativum	—	171, 192
Raphanus sativus	PL	121
Dioscoreaceae		
Dioscorea sativa var. *rotunda*	TU	90
Ericaceae		
Arctostaphylos uva-ursi	PL	169
Rhododendron anthopogon	—	171
Euphorbiaceae		
Euphorbia neriifolia	RT	91
Euphorbia resinifera	—	192
Euphorbia tirucalli	—	171, 192

Table XIII—(*Continued*)

Plant Name	Plant Part[a]	Reference
Excoecaria agallocha	—	192
Stillingia sylvatica	RT	171
Gentianaceae		
Frasera speciosa	PL	90, 92
Gramineae		
Bambusa arundinacea	RT	91
Chusquea ramosissima	YS	92
Dendrocalamus strictus	LF	108, 192
Echinochloa frumentacea	—	171
Guttiferae		
Garcinia morella	—	192
Garcinia pedunculata	—	171
Labiatae		
Lycopus europaeus	LF	115
Lycopus lucidus	PL	121
Ocimum basilicum	LF	92
Ocimum sanctum	LF	99
Origanum majorana	LF	90
Rosmarinus officinalis	PL	90, 92, 115
Salvia plebeia	—	192
Lauraceae		
Cinnamomum cassia	—	192
Lecythidaceae		
Combretodendron africanum	SB	130
Leguminosae		
Astragalus glycyphyllus	PL	132
Cassia lanceolata	—	192
Clitoria ternatea	FR	121
Desmodium retroflexum	—	192
Entada scandens	SD	90, 92
Erythrina variegata var. *occidentalis*	—	171, 192
Gleditsia horrida	FR	137
Piliostigma thonningii	RT	92
Prosopis algarobilla	RT	92
Rhynchosia minima	—	192
Sesbania sesban	FL, LF	102, 171
Vigna phaseoloides	RT	92
Liliaceae		
Aloe barbadensis	LF, FP	102, 116, 192
Asagraea officinalis	SD	171
Asparagus acutifolia	FR	90, 92
Asparagus officinalis	FR	90, 92
Chamaelirium luteum	PL	169
Smilacina stellata	RT, LF	90, 92
Smilax bona-nox	RT	171
Loranthaceae		
Phoradendron flavescens	LF	90
Magnoliaceae		
Magnolia virginiana	BK	171
Malvaceae		
Hibiscus abelmoschus	FL	92
Hibiscus rosa-sinensis	PT	99, 171, 192
Hibiscus tiliaceus	FL	92
Sphaeralcea munroana	RT	92
Urena lobata	LF	90, 92, 192
Melastomataceae		
Memecylon amplexicaule	—	171
Menispermaceae		
Curarea tecunarum	ST	172
Stephania hernandifolia	RZ	102
Musaceae		
Ensete superbum	SD	155
Myristicaceae		
Myristica fragrans	—	192
Virola sp.	ST	101
Myrsinaceae		
Embelia ribes	RT, PL	91, 138
Myrtaceae		
Metrosideros collina	LF	105
Oleaceae		
Jasminum multiflorum	—	171
Palmae		
Cocos nucifera	SD, FJ	90, 92
Licuala sp.	RB	92
Pandanaceae		
Pandanus tectorius	—	171
Papaveraceae		
Argemone glauca	PL, IF	105, 121

(continued)

Table XIII—(*Continued*)

Plant Name	Plant Part[a]	Reference
Phytolaccaceae		
Phytolacca decandra	—	171
Piperaceae		
Piper latifolium	RT	171
Piper leptostachyum	—	171
Piper longum	LF, RT, FR	102, 138, 171, 192
Plantaginaceae		
Plantago lanceolata	PL	90
Polemoniaceae		
Phlox stansburyi	LF	92
Polygonaceae		
Eriogonum jamesii	RT	90, 92
Polygonum hydropiper	RT, PL	90, 157, 158
Polygonum multiflorum	PL	121
Polypodiaceae		
Asplenium adiantum-nigrum	—	90, 92, 171, 192
Dryopteris filix-mas	RT, SD	90, 92, 192
Ranunculaceae		
Aconitum heterophyllum	RT	91
Aconitum napellus	RT	171
Rosaceae		
Geum macrophyllum	LF	92
Hagenia abyssinica	LF, ST	119, 192
Prunus emarginata	WD	92, 117
Pyrus communis	SB	159
Quillaja saponaria	BK	171
Rubus idaeus	LF	169
Sanguisorba officinalis	PL	90, 121, 160
Rubiaceae		
Adinia cordifolia	LF	161
Anthocephalus cadamba	—	171
Anthocephalus indicus	LF, FL	91
Randia dumetorum	FR	103
Randia spinosa	FR	91
Rubia cordifolia	PL	121
Rutaceae		
Evodia rutaecarpa	PL	121
Citrus maxima	—	171
Citrus medica	FR	91
Salicaceae		
Populus alba	SB	90, 92
Santalaceae		
Santalum album	—	192
Sapindaceae		
Sapindus trifoliatus	—	192
Saxifragaceae		
Hydrangea arborescens	RT	171
Schizaeaceae		
Lygodium dichotomum	RT	90, 92
Scrophulariaceae		
Castilleja angustifolia	—	92
Rehmannia glutinosa	PL	121
Solanaceae		
Solanum nigrum	—	192
Tiliaceae		
Triumfetta bartramia	—	192
Umbelliferae		
Anethum sowa	FR	91
Carum carvi	SD, FR	91, 127
Carum roxburghianum	SD	91
Cicuta maculata	RT, RJ	90, 92
Ferula assa-foetida	R	138, 192
Leptotaenia reticulata	—	171
Siler divaricatum	PL	121
Trachyspermum roxburghianum	—	171
Verbenaceae		
Callicarpa macrophylla	—	171
Clerodendrum phlomidis	—	171
Clerodendrum serratum	RT	91
Gmelina asiatica	—	171
Stachytarpheta jamaicensis var. *indica*	—	171, 192
Verbena hastata	PL	171
Vitex lagundi	RT	92
Vitex negundo	SD, RB, RT	90, 91, 192
Zingiberaceae		
Globba marantia	—	92

[a] BK = bark, FJ = fruit juice, FL = flower, FP = fruit pulp, FR = fruit, FS = flower stems, IF = inflorescence, LF = leaf, PL = whole plant, PT = petals, PX = aerial parts, R = resin, RB = root bark, RJ = root juice, RT = root, RZ = rhizome, SB = stem bark, SD = seed, SP = spadix, ST = stem, TU = tuber, WD = wood, and YS = young stems.

ADDENDUM

Three recent papers have come to our attention since the compilation of data reported herein, which we believe should be included in this review.

Kapoor *et al.* (1673) tested extracts of *Areca catechu; Carica papaya, Daucus carota, Mentha arvensis,* and *Polygonum hydropiper,* which had previously been reported to possess antifertility activity, for anovulatory effects in female rabbits. The only plants of this group showing anovulatory activity were the ethanolic extract of *M. arvensis* leaves and the petroleum ether extract of *P. hydropiper* roots.

Similarly, various extracts and chromatographic fractions of the stems and leaves of *Argemone mexicana,* the seeds of *C. papaya,* the seeds of *Lawsonia inermis,* the leaves of *M. arvensis,* and the seeds of *Sapindus trifoliatus* were tested for antifertility activity in female albino rats (1674). The ethanolic extract of *M. arvensis* leaves, as well as certain chromatographic fractions from a methanolic fraction of *S. trifoliatus* seeds, showed high degrees of antifertility activity.

Petroleum ether and aqueous extracts of *Curcuma longa* (Zingiberaceae) rhizomes exerted a 100% antifertility activity in rats at a dose of 200 mg/kg; the effect was not due to anovulatory activity (1675).

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RESEARCH ARTICLES

Release of Corticoids from Oleaginous Ointment Bases Containing Drug in Suspension

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Abstract □ Simplified methods for studying the release of drugs suspended in oleaginous ointment bases were developed. These procedures were used in studying the release rates of two corticoids, fluocinonide and flucloronide, from white petrolatum and petrolatum containing various adjuvants. A practical method for measuring drug solubilities was developed and used in determining solubilities of these corticoids in ointment bases. When using physical data obtained from model ointments, the release rates of drugs from modified ointment bases were predicted. Comparisons of the observed and predicted rates from ointments containing hydrophobic adjuvants indicated the usefulness of the physical model approach in predicting the release rates. For ointments containing emulsifying agents, the simple model used did not provide useful predictions.

Keyphrases □ Fluocinonide—suspension, release from oleaginous ointment bases containing various adjuvants, model predictions □ Flucloronide—suspension, release from oleaginous ointment bases containing various adjuvants, model predictions □ Ointment bases—release of corticoids in suspension □ Release rates—corticoid suspensions from oleaginous ointment bases containing various adjuvants

Percutaneous absorption involves two consecutive steps: the release of the drug from the vehicle and its subsequent penetration through the skin barrier. Generally, the latter step controls percutaneous absorption, because it is the slower of the two events. The release of the drug from the vehicle may play an important role in percutaneous absorption when the drug solubility and its diffusion constant in the vehicle are very small. When the skin barrier is in a damaged state due to disease or injury, drug release from the vehicle then controls percutaneous absorption.

Simplified equations describing the drug release from suspension- (1) and solution- (2) type vehicles have been in the literature for more than a decade. Numerous studies also have attempted to relate vehicle composition to observed changes in the *in vitro* release rate (3–9). Relatively little quantitative information appears in the literature correlating drug release data with variations in physical parameters produced by compositional changes in the formulations. In some cases, the drug release from the vehicles has been complicated by the use of a membrane barrier to separate the donor phase from the receptor phase. The use of dialysis membranes (3), filter membranes (4), membranes of animal origin (5, 6, 8), and dimethyl polysiloxane membranes (7) has been reported.