An Overview of Phytochemical Researches from Korean Medicinal Plants

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In the plant kingdom growing in Korean peninsula, the number of species of higher plants accounts for between 4 and 5 thousand[1]. Of this number less than 900 species have been used for medicinal plants[2] among which include 500 plants in the Korean Pharmacopoeia and the Korean Herbal Pharmacopoeia[3]. Extensive research has been conducted since the early 1940's on isolation and structure elucidation and utilization of the medicinal plants. Till the last year, these include the 239 species, 166 genera and 71 families. Among them the most extensive investigation has been conducted of *Panax ginseng* followed by *Angelica species* and *Phytolacca* species. As listed in Table I, other plants such as *Acanthopanax*, *Aconitum* and *Zizyphus* have also been focused for their phytochemical/biological studies.

Table I. Korean medicinal plants investigated

No. of papers	Genus
> 120	*Panax*
30~40	*Angelica, Phytolacca*
10~20	*Acanthopanax, Codonopsis, Atractylodes, Siegesbeckia, Ginkgo, Polygonum, Aconitum, Zizyphus, Bupleurum*
5~10	*Aralia, Aristolochia, Epimedium, Betula, Melandrium, Euonymus, Artemisia, Euphorbia, Agastache, Perilla, Salvia, Scutellaria, Albizzia, Caragana, Echinosophora, Glycyrrhiza, Fraxinus, Polygala, Paeonia, Duchesnea, Prunus, Rosa, Rubus, Ulmus, Peucedanum*
< 5	*Acer, Alisma, Rhus, Kalopanax, Arisaema, Pinellia, Asarum, Cynanchum, Pycnostelma, Impatiens, Berberis, Corylus, Platycodon, Cannabis, Humulus, Lonicera, Dianthus, Gypsophila, Pseudostellaria, Tripterygium, Chenopodium, Chloranthus, Commelina, Arctium, Aster, Chrysanthemum, Cirsium, Ixeris, Solidago, Taraxacum, Aucuba, Cornus, Brassica, Raphanus, Trichosanthes, Davallia, Dioscorea, Rhododendron, Eucommia, Ricinus, Acalypha, Dipsacus, Quercus, Gentiana, Geranium, Bambusa, Coix, Anemarrhena, Belamcanda, Juncus, Ajuga, Elscholtzia, Leonurus, Mentha, Nepeta, Phlomis, Prunella, Thymus, Akebia, Machilus*

	Continued *Astragalus, Cassia, Gleditschia, Glycine, Lespedeza, Phaseolus, Pueraria, Rovinia, Allium, Liriope, Polygonatum, Smilax, Veratrum, Liriodendron, Magnolia, Melia, Cudrania, Morus, Forsythia, Syringa, Sesamum, Plantago, Dryopteris, Adonis, Erythronium, Caltha, Clematis, Coptis, Lycoctonum, Pulsatilla, Rhamnella, Thalictrum, Chaenomeles, Malus, Potentilla, Sanguisorba, Spiraea, Filipendula, Rubia, Citrus, Dictamnus, Evodia, Poncirus, Zanthoxylum, Thesium, Houttuynia, Astilbe, Rodgersia, Melampyrum, Pedicularis, Scrophularia, Dystaenia, Veronicastrum, Datura, Lycium, Nicotiana, Firmiana, Torreya, Tilia, Typha, Cnidium, Glehnia, Hydrocotyle, Oenanthe, Patrinia, Valeriana, Vitex, Viola, Curcuma*

The number of papers published during the last 5 decades was shown in Table II. As shown in this Table the number of papers published was increased year by year. Especially, from the 1980's the number of papers dramatically increased. During this period, the number of papers published in foreign journals was also increased. But the percentage was about 10% of total numbers.

Table II. Number of papers published in 1948~1994

Year	Domestic journals	Foreign journals	Total
1948~1970	70	1	71
1971~1975	105	6	111
1976~1980	138	18	156
1981~1985	225	17	242
1986~1990	272	51	323
1991~1994	258	27	285
Total	1,068	120	1,188

The summary of classes of isolates from Korean medicinal plants published in domestic journals was categorized as shown in Table III. As would be expected, the majority of these compounds were flavonoids(95/460), followed by triterpenoids(56/460), saponins(47/460), alkaloids(46/460), coumarins (40/460) and sterols(26/460).

Table Ⅲ. Number of papers published in domestic journals

Category of compound	No. of papers	Category of compound	No. of papers
Alkaloid	46	Organic acid	20
Quinone	14	Phenylpropanoid	10
Coumarin	40	Polyacetylene	5
Diterpenoid	13	Saponin	47
Essential oil	18	Sesquiterpene	9
Fatty acid	5	Sterol, steroid	26
Flavonoid	95	Sugar, polysaccharide	6
Glyceride	3	Triterpenoid	56
Iridoid	10	Others	24
Lignan	13	Total	460

The various chemical categories of the new compounds are summerized in Table Ⅳ. As can be seen, of the 190, 123 were compounds reported in foreign journals.

Table Ⅳ. Number of new compounds isolated

Category of compound	Domestic journals	Foreign journals	Total
Akaloid	13	23	36
Coumarin	1	2	3
Diterpenoid	6	3	9
Flavonoid	2	17	19
Iridoid	3	2	5
Lignan	0	7	7
Monoterpene(glycoside)	2	1	3
Phenylpropanoid	4	3	7
Polyacetylene	2	0	2
Saponin	21	37	58
Sesquiterpenoid	4	5	9
Tannin	1	4	5
Triterpenoid	5	12	17
Others	3	7	10
Total	67	123	190

Saponins were most frequently cited, followed by alkaloids, flavonoids and triterpenoids.

A total of 173 articles were published as having one or more types of biological activity in some system(s) having relevance to their potential use as a drug. Of the 173, 24 were articles of foreign journals, and 149 were published in domestic journals. The various categories of biological activity for the compounds are summerized in Table V.

Table V. Biologically active compounds isolated

Name of biological activity	No. of papers	Name of biological activity	No. of papers
Analgesics	3	Antifungal agents	2
Antidiabetics	2	Cytotoxic agents	28(3)
Antifatigue agents	1	Enzyme modifiers	19(4)
Antifertility agents	0(1)*	Hypocholesterolemics	1
Antihelmintics	1	Hypolipemics	1(2)
Antihepatotoxic agents	7(1)	Hypotensives	3
Antiinflammatory agents	20(1)	Immunomodulating agents	1
Antimutagenic agents	1	Nitrite scavenging agents	1
Antioxidants	5(1)	Platelet aggregation inhibitors	5(3)
Antipyretics	2	Sedatives	7
Antithrombotic agents	1	Spasmolytics	2
Antiulcer agents	(1)	Sweet-tasting agents	0(4)
Cardiovascular agents	1	Uremia preventive agents	3
Choleretics	3	Uterine stimulants	1
CNS active agents	4(1)	Miscellaneous	10(2)
Antibacterial agents	9		
Antimicrobial agents	5	Total	149(24)

* Figures in parentheses indicate the number of papers published in foreign journals.

As listed in this Table, various categories of biologically active principles (cytotoxic, antiinflammatory, enzyme modifiers) were most frequently cited, followed by antihepatotoxic, platelet aggregation inhibitors and antioxidants.

Our past research experiences of Korean medicinal plants focused mainly on the isolation and structure elucidation of flavonoids from *Epimedium koreanum, Ginkgo biloba, Lonicera japonica,* and *Zizyphus jujuba,* triterpenoids and their glycosides(saponins) from *Lonicera japonica, Pulsatilla koreana, Caragana sinica, Phytolacca* species, and steroidal saponins from *Smilax china, Liriope spicata* and *Polygonatum sibiricum.* From these medicinal plants, thirty-five new compounds have been isolated and elucidated their structures by means of physicochemical/ spectroscopic methods.

Table VI. Compounds isolated from Korean medicinal plants

Category of compound	No. of compound	Category of compound	No. of compound
Quinone	15(1)*	Lignan	10(3)
Saponin	40(15)	Sesquiterpene	2
Flavonoid	51(6)	Coumarin	10
Iridoid	2	Aromatic acid	3
Hydrocarbon derivatives	7	Triterpenoid	31(7)
Phenylpropanoid	3(2)	Alkaloid	9
Monoterpene(glycoside)	3(1)		
Steroid	7	Total	193(35)

* Figures in parentheses indicate the number of new compounds.

Phytolacca plants are rich in saponins and have been used as a folk medicine for the treatment of edema and rheumatism as well as to cure schistosomiasis. Untill now, we have isolated five new triterpenoids, named esculentic acid[4], jaligonic acid[5], 3-acetylmyricadiol[6]from *P. esculenta* and phytolaccagenic acid[7] and pokeberrygenin[8] from *P. americana* together with the known ones such as phytolaccagenin, acinosolic acid and 3-acetylaleuritolic acid. Eight new saponins named phytolaccosides[9~13]have also been isolated and their structures have been elucidated, among which two major saponins, phytolaccosides B and E exhibited an antiinflammatory activity[14]. A new phenylpropanoid, caffeic aldehyde[15]and three lignans[16,17] have been isolated from the seeds of *Phytolacca* plants. Chemically, the structure of americanin A and D was close similar to the right parts of silybin and silychristin, respectively, the well-known antihepatotoxic agents from

Silybum marianum. Americanin A showed also the antihepatotoxic and antiinflammatory activities[18].

Two novel saponins with antiinflammatory activity, lonicerosides A and B[19] were isolated from the aerial parts of *Lonicera japonica* (Caprifoliaceae) along with ochnaflavone and its 4′-O-methyl ether, quercetin, astragalin, isoquercitrin, rhoifolin, lonicerin, hydnocarpin[20], diosmetin-7-O-glucoside, vogeloside and loganin[21]. The unique biflavonoids, ochnaflavone and its 4′-O-methyl ether exhibited strong inhibitory activity against rat platelet phospholipase A_2[22]. Lonicerin and loganin, a major flavonoid glycoside and iridoid, respectively, showed antiinflammatory activity comparable to aspirin[23].

The BuOH soluble fraction from *Pulsatilla koreana* (Ranunculaceae) was shown to be responsible for the strong sedative activity in a primary experiment. Chromatographic separation/purification gave four hederagenin saponins[24] which were identified as 3-O-α-L-rhamnopyranosyl(1→2)-α-L-arabinopyranoside, 3-O-β-D-glucopyranosyl(1→4)-α-L-arabinopyranoside, 3-O-α-L-rhamnopyranosyl(1→2)-[β-D-glucopyranosyl(1→4)]-α-L-arabinopyranoside 28-O-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranosyl(1→6)-β-D-glucopyranosyl ester.

The major components of root parts from *Caragana sinica* (Leguminosae) were also saponins. A new saponin, caraganoside A was isolated and identified as 3-O-β-D-xylopyranosyl(1→2)[β-D-glucopyranosyl(1→3)]-α-L-arabinopyranosyl oleanolic acid 28-O-β-D-glucopyranosyl ester. Kalopanax-saponin F, hemsloside Ma3 and araloside A were also isolated and characterized[25]

Another large category of saponins, steroidal saponins have been isolated from three liliaceous plants, *Smilax china, Polygonatum sibiricum* and *Liriope spicata*. Investigation of the rhizomes of *Smilax china* has led to isolation of six known diosgenin glycosides, prosapogenin A of dioscin, dioscin, gracillin, methyl protodioscin, methyl protogracillin[26] and methyl proto-prosapogenin A of dioscin[27].

Investigation of the rhizomes of *Polygonatum sibiricum* led to the isolation of the previously reported neoprazerigenin A 3-O-β-lycotetraoside, its methyl proto-type congener, and two new steroidal saponins, sibiricosides A and B. Sibiricogenin, the aglycone of sibiricoside B was a novel compound. The structure of sibiricosides A and B was determined to

be 26-O-β-D-glucopyranosyl-22ξ-O-methyl-25(*S*)- furost-5-ene3β, 26-diol 3-O-β-lycotetraoside and (23*S*,25*R*)-spirost-5-ene-3β, 14α, 23-triol (sibiricogenin)3-O-β-lycotetraoside, respectively[28].

Two novel saponins, spicatosides A and B were isolated from the tubers of *Liriope spicata* and their structures were elucidated as 25(*S*)-ruscogenin 1-O-β-D-glucopyranosyl(1→2)-[β-D-xylopyranosyl(1→3)]-β-D-fucopyran oside and its methyl proto-type, 26-O-β-D-glucopyranosyl 25(*S*)-22ξ-O-methyl furost-5-ene- 1β,3β,26-triol1-O-β-D-glucopyranosyl(1→2)-[β-D-xylopyranosyl(1→3)]-β-D- fucopyranoside[29].

The seeds of *Zizyphus jujuba* (Rhamnaceae) have been used in Chinese medicine for strengthening the nervous system as a remedy for insomnia and sometimes for sleepiness caused both by physical and mental strain. As the constituents of this drug saponins named jujubosides A and B were isolated[30]and recognized to reveal sedative and tranquillizing action in animals[31]. The sedative action of flavonoid fraction was clearly revealed by the hexobarbital-induced hypnosis in mice. The flavone C-glycosides swertisin and spinosin[32]as well as the acylated derivatives of spinosin sinapoyl-, feruloyl- and coumaroylspinosin[33]were isolated and evaluated their activities[34].

In Europe, mainly in Germany and France, but also in other countries of the EC and countries of the EFTA and Asia, there is a large market for phytomedicines based on extracts from the leaves of *Ginkgo biloba* (Ginkgoaceae). The therapeutical properties of *Ginkgo* leaves have been recently reviewed; flavonoids as well as terpenic compounds were regarded as the active constituents[35,36]. The leaves extract of Ginkgo could be assigned to a very complex mixture of flavonoid glycosides. Up to now, twenty-two flavonoid glycosides, six simple flavonoids and six biflavones were identified[37]. Among them, two major flavonol glycosides, kaempferol -and quercetin 3-O-coumaroyl glucosylrhamnosides together with 15 compounds were isolated from the green and yellow leaves of *Ginkgo biloba*[38,39]. During the analysis of these isolates, we reported that the interglycosidic linkage of the aforementioned major flavonol glycosides should be revised as 1→2 rather than 1→4[40]. Our result was confirmed by other research groups such as Markham et al.[41]and Sticher et al.[42]

The aerial parts and underground parts of *Epimedium koreanum* (Berberidaceae) are also rich source in flavonoids[43]. Two new flavonol glycosides, along with epimedoside A, icariin and ikarisoside A, from the

underground parts[44], as well as quercetin, anhydroicaritin 3-O-α-L-rhamnoside and icariin from the aerial parts[45] have been isolated and characterized as 2″-O-rhamnosyl ikarisoside A and 2″-O-rhamnosyl icarisid II. Most of flavonoids isolated from the genus *Epimedium* a prenyl group was attached at C-8 position of the ring A and the interglycosidic linkages such as rhamnosylrhamnose and glucosylrhamnose moieties are 1→2[46] as was previously described in *Ginkgo.*

The roots of *Paeonia albiflora* var. trichocarpa (Ranunculaceae) is one of the important traditional Chinese medicine. The most important constituent is paeoniflorin, a glucoside of a monoterpene of the pinane series. Chromatographic separation of the MeOH extract, in addition to the major constituent paeoniflorin, demonstrated a minor new principle named galloylpaeoniflorin was isolated and structurally determined on the basis of paeoniflorin structure[47]. This compound was also isolated from *P. suffruticosa*[48]. It was inactive in the NCI *in vitro* anti-HIV screening test but showed very strong DPPH radical scavenging effect[48].

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References

1. Lee, Y.N., *Kor.J. Pharmacogn.*, **19**, 53(1988)

2. Ryu, K.S., Yook, C.S. and Hong, N.D., *Kor. J. Pharmacogn.*, **2**, 125(1971)

3. Chi, H.J. and Lee, S.I., *Korean Herbal Pharmacopoeia*, Korean Medical Index Co., Seoul(1988)

4. Woo, W.S. and Kang, S.S., *J. Pharm. Soc. Korea*, **18**, 229(1974)

5. Woo, W.S., *Lloydia*, **36**, 326(1973)

6. Woo, W.S. and Kang, S.S., *Phytochemistry*, **24**, 1116(1985)

7. Woo, W.S. and Kang, S.S., *J. Pharm. Soc. Korea*, **18**, 231(1974)

8. Kang, S.S. and Woo, W.S., *J. Nat. Prod.*, **43**, 510(1980)

9. Woo, W.S. and Kang, S.S., *Phytochemistry*, **15**, 1315(1976)

10. Woo, W.S. and Kang, S.S., *J. Pharm. Soc. Korea*, **21**, 159(1977)

11. Woo, W.S. and Kang, S.S., Wagner, H., Seligmann, O. and Chari, V.M., *Planta Med.*, **34**, 87(1978)

12. Kang, S.S. and Woo, W.S., *Planta Med.*, **53**, 338(1987)

13. Kang, S.S. and Woo, W.S., *Fitoterapia*, **LXII**, 532(1991)

14. Shin, K.H., Woo, W.S. and Lee, C.K., *Kor. J. Pharmacogn.*, **10**, 73(1979)

15. Woo, W.S. and Kang, S.S., *Kor. J. Pharmacogn.*, **10**, 83(1979)

16. Woo, W.S. Kang, S.S., Wagner, H. and Chari, V.M., *Tetrahedron Lett.*, 3239 (1979)

17. Woo, W.S. Kang, S.S., Seligmann, O., Chari, V.M. and Wagner, H., *Tetrahedron Lett.*, **21**, 4255(1980)

18. Lee, E.B., Lee, Y.S. and Woo, W.S., *Arch. Pharm. Res.*, **8**, 139(1985)

19. Son, K.H., Jung, K.Y., Chang, H.W., Kim, H.P. and Kang, S.S., *Phytochemistry*, **35**, 1005(1994)

20. Son, D.H., Park, J.O., Chung, K.C., Chang, H.W., Kim, H.P., Kim, J.S. and Kang, S.S., *Arch. Pharm. Res.*, **15**, 365(1992)

21. Son, K.H., Kim, J.S., Kang, S.S., Kim, H.P. and Chang, H.W., *Kor. J. Pharmacogn.*, **25**, 24(1994)

22. Chang, H.W., Baek, S.H., Chung, K.W., Son, K.H., Kim, H.P. and Kang, S.S., *Biochem. Biophys. Res. Commun.*, **205**, 843(1994)

23. Lee, S.J., Shin, AE.J., Son, K.H., Chang, H.W., Kang, S.S. and Kim, H.P., *Arch Pharm. Res.*, **18**, 133(1005)

24. Kang, S.S., *Arch. Pharm. Res.*, **12**, 42(1989)

25. Lee, Y.B., Yoo, S.S., Kim, J.S. and Kang, S.S., *Arch. Pharm. Res.*, **15**, 62(1992)

26. Kim, S.W., Chung, K.C., Son, K.H. and Kang, S.S., *Kor. J. Pharmacogn.*, **20**, 76(1989)

27. Kim, S.W., Chung, K.C., Son, K.H. and Kang, S.S., *Kor. J. Pharmacogn.*, **20**, 145(1989)

28. Son, K.H., Do, J.C. and Kang, S.S., *J. Nat. Prod.*, **53**, 333(1990)

29. Lee, D.Y., Son, K.H., Do. J.C. and Kang, S.S., *Arch. Pharm. Res.*, **12**, 295(1989)

30. Kawai, K., Akiyama, T., Ogihara, Y. and Shibata, S., *Phytochemistry*, **13**, 2029(1974)

31. Watanabe, I., Saito, H. and Takagi, K., *Japan J. Pharm.*, **23**, 563(1973)

32. Woo, W.S., Kang, S.S., Shim, S.H., Wagner, H., Chari, V.M., Seligmann, O. and Obermeier, G., *Phytochemistry*, **18**, 353(1979)

33. Woo, W.S., Kang, S.S., Wagner, H., Sligmann, O. and Chari, V.M., *Phytochemistry*, **19**, 2791(1980)

34. Woo, W.S., Shin, K.H. and Kang, S.S., *Kor. J. Pharmacogn.*, **11**, 141(1980)

35. Hasler, A., Meier, B. and Sticher, O., *Schweiz. Apotheker-Zeitung*, **128**, 342 (1990)

36. Agnoli, A., Rapin, J.R., Scapagnini, V. and Weitbrecht, W.V., Effetcs of *Ginkgo biloba* extract on organic cerebral impairment, John Libbey, London(1985)

37. Hasler, A. and Sticher, O., *J. Chromatogr.*, **605**, 41(1992)

38. Kang, S.S., Kim, J.S., Kwak, W.J. and Kim, K.H., *Kor. J. Prmacogn.*, **21**, 111(1990)

39. Kang, S.S., Kim, J.S., Lee, M.W. and Lee, D.S., *Kor. J. Pharmacogn.*, **26**, 23(1995)

40. Kang, S.S., Kim, J.S., Kwak, W. J. and Kim, K.H., *Arch. Pharm. Res.*, **13**, 207(1990)

41. Markham, K.R., Geiger, H. and Jaggy, H., *Phytochemistry*, **31**, 1009(1992)

42. Hasler, A., Gross, G.A., Meier, B. and Sticher, O., *Phytochemistry*, **31**, 391(1992)

43. Kang, S.S. and Kim, J.S., *Kor. J. Pharmacogn.*, **22**, 85(1991)

44. Kang, S.S., Kang, Y.J. and Lee, M.W., *J. Nat. Prod.*, **54**, 542(1991)

45. Kang, S.S., Shin, K.H., Chung, S.G. and Cho, E.H., *Kor. J. Pharmacogn.*, **19**, 93(1988)

46. Kang, S.S., *Kor. J. Pharmacogn.*, **23**, 1(1992)

47. Kang, S.S., Shin, K.H. and Chin, H.J., *Arch. Pharm. Res.*, **14**, 52(1991)

48. Yoshikawa, M., Uchida, E., Kawaguchi, A., Kitagawa, I. and Yamahara, *J.*, *Chem. Pharm. Bull.*, **40**, 2248(1992)