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Naphthaquinones from some Boraginaceous Taxa - A Chemical Review

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Abstract – The naphthaquinones - isohexenylnaphthazarins - are mostly found in the ceratenchymatous cells of the roots of some boraginaceous taxa. A total of 34 naphthazarins and their derivatives have been isolated from these taxa till date.

Key words – Boraginaceous taxa, ceratenchyma, naphthaquinone, review.

Introduction

The majority of naphthalene derivatives present in nature are quinones and are usually found in the ceratenchyma of the roots of about 150 plant species mostly belonging to the family Boraginaceae. Now, it has been proved beyond doubt that not only red coloration of the roots of the boraginaceous taxa but also their therapeutic actions are due to the presence of napthaquinones - isohexenylnaphthazarins. Various workers have observed antibacterial, anticancer, antiinflammatory, antifungal, antiplatelet, and wound healing properties of these components [Bhakuni *et al.* (1969); Chang *et al.* (1993); Hayashi and Fukushima (1979); Honda *et al.* (1988); Katti *et al.* (1979); Konoshima and Kozuka (1989); Lin *et al.* (1980); Nadir *et al.* (1986); Papageorgiou (1980); Papageorgiou *et al.* (1980); Sankawa *et al.* (1977, 1981) and Seshadri *et al.* (1985)]. A number of cosmetics, dyes, pharmaceutical preparations, and food colorants have also been prepared from time to time either from the isohexenylnaphthazarin pigments and their derivatives or directly from the crude plant extract having these naphthaquinones [Futagoishi and Abe (1972); Hasegawa *et al.* (1987); Hatinguais and Belle (1980); Inoue *et al.* (1986); Kishimoto and Aota (1977); Kozo *et al.* (1950, 1951); Matsui *et al.* (1973, 1977, 1978); Motoyama and Ishitoku (1991); Nakazono (1985); Papageorgiou (1978); Tabata and Honda (1987)].

Due to the various properties and importance attributed to these isohexenylnaphthazarins, many workers throughout the world have isolated and identified these naphthaquinones from the species of the genera-*Alkanna, Anchusa, Arnebia, Echium, Lithospermum, Macrotomia, Maharanga*, and *Onosma*. In the present paper, an attempt has been made to present a systematic and comprehensive review on these compounds.

Review

Papageorgiou (1980) described the chemistry, biosynthesis, biological properties and wound healing activity of some of the isohexenylnaphthazarins, commonly known as alkannins. In this presentation all the papers dealing with the naphthaquinons isolated from the boraginaceous taxa are arranged in tabular form along with their chemical struc-

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tures and plant sources with relevant references (in parenthesis). Besides, an effort has also been made to include the work on the qualitative and quantitative parameters of naphthaquinons and is being given below.

Rukuzin and Pekarskava (1916) studied the adsorption property of alkannins for different solvents and found that the benzene soluble alkannins were completely adsorbed by animal charcoal within an hour while these were not at all adsorbed by phenylamine. Further, it was observed by Betrabet and Chakravarti (1933) that this alkannin naphthazarin reacted with different chemical reagents to yield its derivatives viz. tetra-acetate-, dimethoxy-, tetrabenzoyl-, dimethoxydibenzoyl-, dicarboxy-, hexabromo-, tetrabromo-, tetra-acetyltetrabromo-, dinitrotetra-acetyl naphthazarin and β-methyl-anthracene.

Chaisukasant *et al.* (1993) applied glassy carbon electrode method for determination of total alkannins from the roots of *Alkanna tinctoria*. A quantitative determination of total alkannins in whole root, root bark and lower (mature) leaves of *Onosma echioides* was carried out by Boldyrev (1940), and found to be 8.93, 19.41 and 2.52% respectively, while in the roots of *Arnebia euchroma, A. guttata* and *Lithospermum erythrorhizon*, it was 1.11-4.98, 0.83-4.90 and 1.57-2. 38% respectively.

Xue and Xu (1990) extracted the shikonin-an antipode of alkannin - from the roots of *L. erythrorhizon* and described its physicochemical properties. The qualitative and quantitative evaluation of naphthaquinones in the boraginaceous taxa was studied by Tareeva *et al.* (1970), Kagramanyan and Mnatsakanyan (1985) and Zhang *et al.* (1989). They estimated total shikonin in *Arnebia tibetana* (4.16%), *A. euchroma* (2.45%), *Lithospermum erythrorhizon* (2.33%), *Macrotomia* sp. 2.21%), *Onosma setosum* (0.07%) and *O. zerizaminum* (1.59%). The variation of shikonin content in the subterranean parts of *Macrotomia euchroma* within the plants of different ages was also studied by Pinenova and Tareeva (1980) and the maximum amount was detected during the reproductive phase of the plants.

Besides, the isolation, identification and elucidation of structure of alkannin and shikonin, Brockmann (1935) also showed that these isohexenyl naphthazarins could be converted into an identical optically inactive monomethyl ether and in combination, yielded the racemic compound shikalkin, m.p. 148°. Similarly Shcherbanovskii (1971) estimated the total amount of shikalkin in the young and old specimens of *Onosma visianii* as 0.52 and 0.35% respectively. Moruzzi (1939) determined the oxidation-reduction potential of the above two isomers of the naphthazarin, alkannin.

Sankawa *et al.* (1977) isolated alkannane together with some other compounds from the roots of *Macrotomia euchroma*. Later, in 1981 they clarified that the isohexenyl naphthazarin pigments obtained from the 'Nan-Shikon' (*Macrotomia euchroma*) were the derivatives of alkannin instead of shikonin on the basis of the reports of Tsukada *et al.* (1980). They also obtained cycloalkannin, cycloalkannin leucoacetate, alkannae leucoacetate and cycloalkannin diacetate.

Sung *et al.* (1980) carried out the quantitative determination of β β-dimethylacryl-shikonin from some Chinese medicinal plants viz. *Arnebia euchroma, A. guttata, Lithospermum erythrorhizon, Onosma hookeri* and *O. paniculata* and it was found to be 2.4-3.6; 1.21; 0.27; 0.75-0.92 and 0.132-1.0% respectively. The total estimation of the above naphthaquinone could also be done by HPLC with cell calibration method according to Lin *et al.* (1995).

Kuroda and Wada (1938) synthesized the alkyl derivatives of naphthazarins, naphthopurpurin and their related compounds from the roots of *Lithospermum erythrorhizon*. Manabe *et al.* (1987) developed a procedure

Table I. Presence of Naphthaquinones in Various Plant Species

S. No.	Name of the compound	R	R_1 (Side chain)**	Plant species
* 1.	β-Acetoxyisovalerylalkannin	H	– CH. $CH_2CH{=}CMe_2$ O. Co. CH_2. C(O. CO. CH_3)Me_2	*Alcanna tinctoria* [65]; *Arnebia euchroma* [14, 15]
2.	β-Acetoxyisovalerylshikonin	H	– CH. $CH_2CH{=}CMe_2$ O. CO. CH_2. C(O. CO. CH_3)Me_2	*Macrotomia euchroma* [12].
* 3.	Acetyl alkannin or Arnebin-3	H	– CH. $CH_2CH{=}CMe_2$ O. CO. CH_3	*Alkanna tinctoria* [67]; Arnebia euchroma [32, 15]; *A. hispidissima* [31, 17]; *A. nobilis* [65, 32]; *Macrotomia cephalotes* [65]; *Lithospermum Officinale* [35]; *Onosma hispidum* [32].
* 4.	Acetyl-hydroxy-alkannin or Arnebin-6	H	– CH. CH_2. CH_2. C(OH)Me_2 O. CO. CH_3	*Arnibia benthamii* [32], *A. euchroma* [32], *A. nobilis* [65, 32], *Maharanga emodi* [32].
* 5.	Acetylshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_3	*Arnebia decumbens* [1]. *A. euchroma* [10, 14, 15, 53, 91, 95]; *Lithospermum arvense* [11], *L. erythrorhizon* [21, 41, 42]; Onosma confertum [3], *O. echioides* var. *hispidum* [38], *O. paniculata* [53], *O. setosum* [28].
* 6.	Alkannan	H	– CH_2. CH_2. CH_2. $CHMe_2$	*Alkanna tinctoria* [65]; *Macrotomia euchroma* [74]
* 7.	Alkannin or Arnebin-4 (Laevorotatory)	H	– CH. CH_2. CH=CMe_2 OH	*Alkanna tinctoria* [5, 8, 59, 65]; *Arnebia euchroma* [32, 50]; *A. guttata* [46], *A. hispidissima* [31], *A. nobilis* [32, 65, 82]; *Echium humuli, E. longifolium* [90]; *Lithospermum arvense* [65], *L. erythrorhizon* [46], *L. officinale* var. *erythrorhizon* [75], *Maharanga emodi* [32], *Onosma echioides* [7], *O. hispidum* [32]. *Alkanna tinctoria* [65].
* 8.	Angelicalkannin	H	– CH. CH_2. CH=CMe_2 O. CO. C(Me)=CHMe	*Alkanna hirsutissima* [65].
* 9.	Angelicshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. C(Me)=CHMe	*Lithospermum erythrorhizon* [4]; *Macrotomia euchromon* [45]. *Lithospermum euchromum* [36].
*10.	Anhydroalkannin	H	– CH-CH. CH=CMe_2	*Alkanna hirsutissima*, *A. tinctoria*; *Macrotomia*
11.	Dehydroxyshikonin	H	– CH=CH. CH=CMe_2	*cephalotes* [65]; *Onosma heterophylla* [58]
*12.	Deoxyalkannin	H	– CH_2. CH_2. CH=CMe_2	*Arnebia benthamii* [32], *A. euchroma* [14, 15, 32, 53, 91, 95]; *A. guttata* [51, 95], *A. hispidissima* [31], *A. nobilis* [32, 65];
*13.	Deoxyshikonin or Arnebin-7	H	– CH_2. CH_2. CH=CMe_2	*Lithospermum erythrorhizon* [1, 21, 42] *L. euchromum* [36]; *Macrotomia euchroma* [65]; *Onosma confertum* [3], *O. hispidum* [32], *O. paniculata* [53].

Table I. Continued

S. No.	Name of the compound	R	R_1 (Side chain)	Plant species
*14.	β, β-Dimethylacrylalkannin or Arnebin-1	H	– CH. CH_2. CH=CMe_2 O. CO. CH=CMe_2	*Alkanna tinctoria* [65]; *Arnebia euchroma* [14, 15, 32, 50], *A. hispidissima* [17], **A. nobilis* [32, 65]; **Macrotomia cephalotes* [65]; *Onosma heterophylla* [58], *O. hispidum* [32].
*15.	β, β-Dimethylacryl-hydroxy-alkannin or Arnebin-2	H	– CH. CH_2. CH_2. C(OH)Me_2 O. CO. CH=CMe_2	*Arnebia euchroma* [32], **A. nobilis* [32, 82, 83]; *Maharanga emodi, Onosma hispidum* [32].
*16.	β, β-Dimethylacryl shikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH=CMe_2	*Alkanna hirsutissima* [2]; *Arnebia benthamii* [32], *A. euchroma* [10, 32, 53, 91, 95], *A. guttata* [95]; **Lithospermum erythrorhizon* [65]; *Maharanga emodi* [32]; *Onosma confertum* [3], *O. hispidum* [32], *O. hookerii, O. paniculata* [84].
*17.	Hydroxy-alkannan or Arnebin-5	H	– CH_2. CH_2. CH_2. C(OH)Me_2	*Arnebia euchroma* [32], **A. nobilis* [32, 65]; *Maharanga emodi* & *Onosma hispidum* [32].
*18.	β-Hydroxyisovlerylalkannin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_2. C(OH) Me_2	*Arnebia euchroma* [15], *A. hispidissima* [31].
*19.	β-Hydroxyisovalerylshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_2. C(OH) Me_2	*Arnebia euchroma* [91, 95], *A. guttata* [51, 95]; *Lithospermum arvense* [11], **L. erythrorhizon* [4, 21, 24, 65], *L. officinale* [35].
*20.	Isobutylshikonin	H	– CH. CH_2. CH=CMe_2 O. CH_2. $CHMe_2$	**Lithospermum erythrorhizon* [23, 65], *L. officinale* [35].
21.	Isobutyrylshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. $CHMe_2$	*Lithospermum arvense* [11], *L. erythrorhizon* [13, 42].
*22.	Isovalerylalkannin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_2. $CHMe_2$	**Alkanna tinctoria* & **Macrotomia cephalotes* [65]; *Onosma heterophylla* [58].
*23.	Isovalerylshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_2. $CHMe_2$	**Arnebia decumbens* [1]; **Lithospermum arvense* [11]; **L. erythrorhizon* [13, 21, 41, 42, 65].
24.	1-Methoxyacetylshikonin	Me	– CH. CH_2. CH=CMe_2 O. CO. CH_3	*Arnebia euchroma* [15].
*25.	α-Methyl-n-butyl-alkannin	H	– CH. CH_2. CH=CMe_2 O. CH(Me). CH_2. CH_2 Me	*Macrotomia cephalotes* [65].
*26.	α-Methyl-n-butyl-shikonin	H	– CH. CH_2. CH=CMe_2 O. CH(Me). CH_2. CH_2 Me	*Lithospermum erythrorhizon* [65].

Table I. *Continued*

S. No.	Name of the compound	R	R_1 (Side chain)	Plant species
*27.	α-Methyl-n-butyryl-shikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH(Me). CH_2Me	*Lithospermum erythrorhizon* [21].
28.	Onosone A	Me	– CH. CH_2. CH=CMe_2 OH	*Onosma hispidum* [30].
29.	Onosone B	Me	– CH. CH_2. CH=CMe_2 O. CO. CH=CMe_2	*Onosma hispidum* [30].
30.	Propionylshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_2. CH_3	*Lithospermum erythrorhizon* [13].
31.	Propylshikonin	H	– CH. CH_2. CH=CMe_2 O. CH_2. CH_2. CH_3	*Lithospermum erythrorhizon* [41].
32.	Shikalkin or DL Shikonin	H	– CH. CH_2. CH=CMe_2 OH	*Arnebia hispidissima* [17]; *Echium italicum* [81], *E. lycopsis* [80] *E. vulgare* [81]; *Macrotomia euchroma* [74]; *Onosma polyphyllum* & *O. visianii* [77].
*33.	Shikonin (Dextrorotatory)	H	– CH. CH_2. CH=CMe_2 *OH*	*Arnebia benthamii* [32], *A. decumbens* [1], *A. euchroma* [32, 95] *A. guttata* [51, 95], *A. tibetana* [69, 71]; *Echium rubrum* [71]; *Echium* spp [81]; ※*Lithospermum erythrorhizon* [21, 23, 24, 42, 43, 59, 65], *L. euchromum* [24], Echium rubrum [71]; Echium spp [81]; **Lithospermum* **L. officinale*; *Macrotomia echioides* [72], *M. euchroma* [70]; *Onosma caucasicum* [71], *O. confertum* [3] *O. hispidum* [32], *O. livanovii* [72] *O. polyphyllum* [79], *O. sericeum*, *O. setosum* [72]; *O. tauricum* [78] *O. visianii* [77], *O. zerizaminum* [86].
*34.	Teracrylshikonin	H	– CH. CH_2. CH=CMe_2 O. CO. CH_2. C(Me)=CMe_2	*Arnebia euchroma* [10, 91, 95], *A. guttata* [95], **Lithospermum euchromum* [24], *L. officinale* [35].

*Note: Also mentioned by Papageorgiou [65].
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to extract the shikonin derivatives from the roots of *Lithospermum sps.* with super critical carbon dioxide without using entrainer (ethanol or water). Papageorgiou *et al.* (1985) used TLC for quantitative determination of isohexenyl-naphthazarin pigments. Luo & Li (1992) also determined the naphthaquinones in 'Zicao' (a Chinese medicine) from different origins (eg. *Arnebia euchroma, A. guttata, Lithospermum erythrorhizon* and *Onosma paniculata* by using TLC at 523 nm, the total naphthaquinone pigments in the above three species except *O. paniculata* was also calculated by calorimeteric method at 517 nm.

Verma and Dass (1959) presented a report on a new acid-base indicator obtained from alcoholic extractive of 'Ratanjot' which became pinkish red in acid and bluish violet in alkaline medium and the pH interval for the colour change was 7.5 to 8.8. Nigam and Mitra (1964) extracted the colouring matter from the two different plants viz. *Arnebia hispidissima* and Market sample** of 'Ratanjot' and found that the pigments of *A. hispidissima* were 78% soluble in fat, while 93% in the case of market sample, however, U.V. spectrum (at 280 and 520 nm) was approximately the same for both the samples.

The decrease of shikonin derivatives was examined in the roots of *Lithospermum erythrorhizon* during preservation at a sunny window side in glass bottles using HPLC by Yoshizaki & Hisamichi (1983). Ikenaga *et al.* (1986, 1989) observed the seasonal changes with in the plant growth in naphtha- quinone pigments (shikonin derivatives) contents and pigment yield of *L. erythrorhizon.* The pigment yield reached a maximum in November for both one year and two year old plants, although it was greater in the latter. Similarly, the effect of temperature showed that the plant growth and the pigment yield increased at a night temperature of 25°.

** Species not mentioned

Tsukada *et al.* (1983) studied 42 commercial samples of the crude 'Shikon', mostly originating from Japan, China, Hongkong and Korea, for their red naphthaquinone pigment contents. Morphologically these samples belong to the 'Ko-shikon' which is probably the roots of *L. erythrorhizon* or 'Nanshikon' attributable to the roots of *Arnebia euchroma.* The total pigment content varied widely, ranging from 0.1-7.7% in 'Nanshikon' (23 samples) and from 0.5-3.2% in 'Ko-shikon' (19 samples). Some of the 'Ko-shikon' samples containing alkannin derivatives might be the roots of some other boraginaceous species.

Recently, Khatoon *et al.* (1993) have identified seven commercial samples of a crude drug 'Ratanjot' by comparing them with the authenticated materials collected from different Himalayan regions (*Arnebia benthamii, A. euchroma, A. nobilis, Maharanga emodi* and *Onosma hispidum*) with the help of TLC fluorescence fingerprinting and found that all the market samples were the mixture of two or three taxa except for the Amritsar sample which was identifide as *Arnebia nobilis.*

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References

Afzal, M., Ghalib, Al-Oriquat, Shikonin derivatives. VI. Chemical investigation of *Arnebia decumbens., Agric. Biol. Chem.*, **50**(6), 161-165 (1986).

Afzal, M. and Mohammad, N., Shikonin B, β-dimethylacrylate, a component of *Alkanna hir-*

sutissima, Agric., Biol, Chem, **47**, 411-412 (1983).

Ai, Kehui, Li, F., Li, Yong, Wang, Weibo and Wu, Yurong, Naphthaquinone constituents of *Onsoma confertum* W. W. Smith and quantitative determination of shikonin. *Zhiwu Xuebao* **31**, 549-53, (1990). [Chem. Abst., 112. 115753 w (1990)].

Bai, Guang and Jin, Xiang-jun, Chemical constitutents of *Lithospermum erythrorhizon. Chem. Res. Chin, Univ.* **10**, 263-265, (1995). [Chem. Abst., 122, 183145 h (1995)].

Betrabet, V. M. and Chakravarti, G. C., Coloring constituents of alkanet root (*Anchusa tinctoria*). 1. Constitution of alkannin II constituents of the wax from alkanet root. *J. Indian Inst. Sci.*, 16A, 41-51; 52-53 (1933).

Bhakuni, D. S., Dhar, M. L., Dhar, M. M., Dhawan, B. N. and Mehrotra, B. N., Screening of Indian Plants for biological activity. Part II. *Indian J. Exp. Biol.*, **7**, 250-262 (1969).

Boldyrev. N. N., A Soviet alkannin. *Khim, Referat. Zhur.* **5**, 108 (1940).

Brockmann, H., Constitution of alkanin, shikonin and alkannan. *Annalen*, **521**, 1-17 (1935).

Chaisukasant, R., Voulgaropoulous, A., Mellidis, A. S. and Papageorgiou, V. P., Voltametric determination of total alkannin using a glassy carbon electrode. *Analyst* (Cambridge, U.K.), **118**, 179-182. [Chem. Abst. **118**, 198309 d (1993)].

Chang, Yuan Shium, Kuo, Sheng Chu, Weng, Szu-Hsin, Jan, Shiuh Chuan, Ko, Feng Nien and Che, Ming, Inhibition of platelet aggregation by shikonin derivatives isolated from *Arnebia euchroma. Planta Med.*, **59**, 401-404 (1993).

Cisowski, W., Dembinska-Migas, Wanda and Dzikowska, Jadwia, Naphthaquinone dyes from the root of *Lithospermum arvense. Acta Pol. Pharm.*, **50**, 443-446 (1993). [Chem. Abst. 121, 200860 j (1994)].

Cong, P. Z., Mass spectrometeric studies on alkannins. *Acta Pharm. Sin.*, **19**(6), 450-454 (1984).

Fedoreyev, S. A., Denisenko, V. A., Kulesh, N, I., Krasovskaya, N. P., Kozyrenko, M. M., Bulgakov, V. P. and Zhuravelev, Yu. N., Examining the chemical composition of quinoid pigments from *Lithospermum erythrorhizon* Seib. et Zucc. cell cultures BK-39. *Khim. Farm. Zh.*, **27**, 33-37 (1993). [Chem. Abst., 120, 240061 (1994)].

Fu, S. L., Shang, T. N. and Xiao, P. G., Analysis of, naphthaquinone pigments in some Chinese medicinal 'Ziaco', *Arnebia euchroma. Acta Pharm. Sin.*, **19**(12), 921-925 (1984).

Fu, S. L. and Xiao, P. G., Naphthaquinone pigments in Xinjing Ruanzicao (*Arnebia euchroma*). *Zhongcaoyao*, 17(10), 434-437 (1986), [Chem. Abst., 106, 55728 f (1987)].

Futagoishi, H. and Abe, T., Application of extract of *Lithospermum* radix to cosmetics. *Cosmet. Perfum.*, 88(1), 51-53 (1972). [Chem. Abst., 76, 128376 e (1972)].

Hamdard, M. E., Badar Y., Khan, M. S. Y. and Shamsi, M. A., Revised phytochemical study of *Arnebia hispidissima. Pak. J. Pharm. Sci.*, 1(1), 19-20 (988). [Chem. Abst, 109, 146300 p (1988)].

Hasegawa, K., Nakajima, Tsuyoshi, T., Horiuchi, T. and Inoue, Y., Pharmaceutical transdermal taps for oral cavity. *Jpn. Kokai Tokai Tokkyo Koho* JP 62, 255, 417 (87, 255, 417), 199 pp (1987). [Chem. Abst., 109, 19717 q (1988)].

Hatinguais, P. and Belle, R., Hair coloring composition containing *Alkanna tinctoria* extract. *Fr. Demande* FR. 2, 477, 872 (Cl. A61 K7/13), 9 pp. (1980). [Chem. Abst., 96, 11513 c (1982)].

Hayashi, Teruaki and Fukushima. M., Pharmaceutical containing extracts of *Ligusticum acutilobum* and *Lithospermum officinale* for skin diseases. *Jpn. Kokai Tokkyo Koho* 79, 89, 013 (Cl. A 61 K 35/78), Appl. 77/156, 447, 27, Dec. 1977. 4pp. (1979). [Chem. Abst., 92, p 47223 q (1980)].

Hisamichi, S. and Yoshizaki, F., Studies on Shikon I. Structure of new minor pigments and isolation of two isomers of shikonin derivatives from *Lithospermum erythrorhizon* Sieb. Zucc. *Shoyakugaku Zasshi*, 36(2), 154-159 (1982). [Chem. Abst., 97, 178739 p (1982)].

Honda, G. Sakakbara, F., Yazaki, K. and Tabata, M., Isolation of deoxyshikonin, an antidermatophytic principle from *Lithospermum erythrorhizon* cell cultures. *J. Nat. Prod.*, **51**, 152-154 (1988).

Ichiro, M., Tokiko, K. Shigeri, I. and Yoshimasa, H., Naphthaquinone derivatives from *Lithospermum erythrorhizon. Tetrahedron Letters*, **52**, 4737-4739 (1965).

Ichiro, M. and Yoshimasa, H., Naphthaquinone derivatives from *Lithospermum erythrorhizon. Tetrahedron Letters*, **31**, 3677-3680 (1966).

Ikenaga, T., Kikuta, S., Mimura, K. and Ohashi, H., Growth and naphthaquinone pigment production in *Lithospermum erythrorhizon* Seib. and Zucc.: I

Seasonal changes. *Shoyakugaku zasshi*, 40(4), 397-400 (1986). [Biol. Abst., 83, 121131 (1987)].

Ikenaga, T. Mimura, K., Ohasi, H. and Kikuta, S., Growth and naphthaquinone pigment production in *Lithospermum erythrorhizon*: II. Effect of night temperature. *Shoyakugaku Zasshi*, 43, 83-85 (1989). [Chem. Abst. 111, 130887 r (1989)].

Inoue, Y., Horiuchi, T., Hasegawa, K., Nakashima, K. and Ysuyoshi, T. Adhesive oral bandages and oral pharmaceutical preparations. *Eur. Pat.* Appl. EP 200, 508 JP Appl. 85/91, 580, 25 pp (1986). [Chem. Abst. 107, 12916 e (1987)].

Kagramanyan, N. S. and Mnatsakanyan, V. A. Shikonin and its dervatives from *Onosma setosum* roots. *Arm. Khim. Zh.*, **38** (8), 527-528 (1985). [Chem. Abst., 104, 65918 r (1986)].

Katti, S. B, Shukla, Y. N. and Tandon, J. S., Arnebin derivatives for anticancer activity. *Indian J. Chem.* **18B**, 440-442 (1979).

Khajuria, P. K. and Jain, S. M., Two new naphthaquinones from the roots of *Onosma hispidun. Indian J. Chem.* Sect. B., 32, 390-391 (1993).

Khan, H. A., Chandrsekharan, I. and Ghanim, A., Naphthazarins from *Arnebia hispidissima. Phytochem.* **22**(2), 614-615 (1983).

Khatoon, Sayyada (1991). Ph. D. Thesis entitled *Pharmacognostic and Chemotaxonomic studies of Indian 'Ratanjot'* (Awarded from Aligarh Muslim University, Aligarh, U.P., India).

Khatoon, Sayyada, Mehrotra, S., Shome, U. and Mehrotra, B. N., Analysis of commercial 'Ratanjot' by TLC Fluorescence fingerprinting. *Int. J. Pharmacog.*, **31**(4), 269-277 (1993).

Kishimoto, S. and Aota, K., *Lithospermum officinale* extracts for skin cosmetics. *Japan Kokai* 74, 124, 218, 3pp. (1974). [Chem. Abst., 82, 160218y (1975)].

Kishimoto, S. and Aota, K., *Lithospermum officinale* extracts for skin cosmetics. *Japan Kokai* 77, 27, 692, (Cl. A 61 K7/00) Appl. 74/35 835, 3pp (1977). [Chem. Abst., 87, 189309t (1977)].

Komatsu, M., Kyogoku, K., Suzuki, T., Tachi, Y. and Terayama, H., Dehydroxyshikonin. *Japan Kokai* 74, 48, 811, 3pp. (1972). [Chem. Abst., 83, 58529j (1975)].

Konoshima, T., Kozuka, M., Koyama, J., Okatani, Tgahara, K. and Tokuda, H., Studies on inhibitors of skin tumor promotion, VI. Inhibitory effects of quinones on Epstein-Barr Virus activation. *J. Nat. Prod.* **52**, 987-995 (1989).

Koul, S., Sambyal, M., Khajuria, R. K. and Jain, S. M., Acetylshikonin from cell cultures of *Onosma echioides* var. *hispidum. Fitoterapia*, **64**, 552-553 (1993).

Kozo, Hayashi, Tachika, Isaka and Suzushino, Gon, Chemical identification of vegetable dyes usd on ancient Japanese silk (a preliminary report). *Misc. Reps, Research Inst. Nat. Resources* No. 17-18, 33-42 (1950). [Chem. Abst., 47, 6660g (1953)].

Kozo, Hayashi, Tachika, Isaka and Suzushino, Gon, Chemical studies of the vegetable dyes on the silk fragment found in Fujiwara's coffins at the chuson Temple. *Misc. Reps. Research Inst. Nat. Resources* No. 24, 60-64 (1951). [Chem. Abst., 47, 870b (1953)].

Kozyrenko, M. M., Bulgakov, V. P. Zhuravlev, Yu. N. and Fedoreev, S. A., Biosynthesis of shikonin derivatives in callus culture of *Lithospermum erythrorhizon* Seib. et. Zucc. *Rastit Resur*, 27, 78, [Chem. Abst., 117, 110038k (1992)].

Krivoshchekova, O. E., Fedoreev, S. A., Denisenko, V. A., Maksimov, O. B. and Gerovoi, P. G., Napthaquinones of *Lithospermum erythrorhizon. Khim. Prir. Soedin*, 1976 (6), 726-730 (1976). [Chem. Abst., 86, 86122b (1977)].

Kuroda, C., The colouring matter in *Lithospermum erythrorhizom. Kwagaku Swaishi* (J. Tokyo Chem. Soc.), 39, 1051-1115 (1918). [Chem. Abst., 13, 713^{6} (1919)].

Kuroda, T. and Wada, M. Constituents of shikonin II. synthesis of alkyl derivatives of naphthazarin, naphthopurpurin and their related compounds. *Sci. Papers Inst. Phys. Chem. Research* 34, 1740-1746 (1938). [Chem. Abst., 33, 2511^{3} (1939)].

Kyogoku, K., Terayama, H., Tachi. Y., Suzuki, T. and Komatsu, M., Constituents of Skikon II. Comparison of contents, constituents, and antibacterial effect of fat soluble fraction between Nan shikon and Koshikon. *Shoyakugaku Zasshi*, 27(1), 31-36 (1973). [Chem. Abst., 80, 52315c (1974)].

Li. Z., Zhang, Min and Guo, Lanjian, determination of alkannin in Zicao (radix arnebiae or Lithospermi). *Yaowu Fenxi Zashi*, 6(1), 42 (1986). [Chem. Abst., 104, 165410n (1986)].

Lin, Shibiao, Skin tonic cream containing hypocrellin. *Faming Zhuanli Shenquing Gongkai Shuomingshu*, CN 85, 103, 693 Appl. 18 May, 1985, 6pp. (1986). [Chem. Abst. 108, 81819x (1988)].

Lin, Zhi-Bin, Chai, Bao-Ling, Wang, Pei, Guo, Qian-

Xing, Lu, Fu-Sun and Xiang, Gui-Qiong, Studies on the anti-inflammatory effect of chemical principle of Zicao (*Arnebia euchroma*). *Pri-Ching I Hsuch Yuan Husch Pao*, 12(2) 101-106 (1980). [Chem. Abst. 93, 143008q (1980)].

Lin, L. X., Han, J. Y., Fan, M. F. and Lin, K. D., Quantitation of β, β-dimethylacrylshikonin in gromwell by HPLC with flow cell calibration method. *Yaoxue Xuebao* 30, 123-26 (1995). [Chem. Abst., 122, 248473 h (1995)].

Liu, Guo-Sheng, Isolation and identification of alkannin B. B-dimethyacrylate, a new naphthaquinone component in *Arnebia euchroma* Johnst. *Yao Hsuch Tung Pao*, **16**(5), 14-15 (1981). [Chem. Abst., 95, 156425q (1981)].

Lu, F., Xiang, Q. and Zhu, F., Studies on the chemical constituents of *Arnebia guttata*. *Zhiwa Xuebao* **25**(5), 455-459 (1983). [Chem. Abst., 100, 99960f (1984)].

Luo, S. and Li, T., Determination of naphthaquinone in Zicao. *Zhongyao Zazhi* **17**, 552-554 (1992). [Chem. Abst., 118, 154683s (1993)].

Luo, S. R. and Li, T., Determination of naphthaquinones in tissue cultured Zicao. *Yoaxue Xuebao*, **26**, 953-955 (1991). [Chem. Abst., 116, 221670j (1992)].

Manabe, A., Tokumori, T., Sumida, Y., Yoshida, T., Hatano T., Yazaki, K. and Okuda, T., Application of supercritical fluid extraction to components of crude drugs and plants. III. Extraction of pigments from *Lithospermum* root and licorice root. *Yakugaku Zasshi* **107**(7), 506-510 (1987). [Chem. Abst., 107, 205004d (1987)].

Matsui, Kenji, Ando, H. and Endo, T. Extract of *Lithospermum* for cosmetics. *Japan Kokai* 77, 39, 884 (Cl. A 61 K 35/78), Appl. 73/99, 725, 5pp (9173) [Chem. Abst., 80, 27680a (1974)].

Matsui, Kenji, Ando, H. and Endo, T., *Lithospermum* extracts for cosmetic preparations. *Japan Kokai* 77, 94, 432 (Cl. A 61 K 7/26). 8pp. (1977). [Chem. Abst., 88, 27680a (1978)].

Matsui, Kenji, Endo, T. and Ando, H., *Lithospermum* extract for liquid cosmetics. *Japan Kokai* 78, 08, 767 (Cl. A 61 K 38/78) Appl. 73/99, 726, 3pp. (1978). [Chem. Abst., 89, 11960b (1978)].

Mellidis, A. S. and Papageorgiou, V. P., Naphthazarins from *Onosma heterophylla*. *J. Nat. Prod. (Lloydia)*, **50**(4), 618-619 (1987).

Moruzzi, G., Oxidation reduction potentials of natural substances of the naththaquinone group. *Mem. Accad. Sci. Ist. Bologna Classe Sci. Fis.*, 6, 61-69 (1930). [Chem. Abst., 36, 3473P^8 (1942)].

Motoyama, Y. and Ishitoku, T., Extraction of shikonin from *Lithospermum erythrorhizon., Jpn.* Kokai Tokkyo Koho JP 03, 27, 342 (91, 27, 342), Appl. 89/163, 352 (1991). [Chem. Abst., 115, P 5306g (1991)].

Nadir, M. T., Dhahir, A. B. J., Al-Serraj, S. M. and Hussain, W. A., The effect of different methods of extraction on the antimicrobial activity of medicinal plants. *Fitoterapia*, **57**, 359-363 (1986)].

Nakazono, S., Manufacture of natural food colors. *Jpn. Kokai Tokkyo Koho JP*60, 262, 569 [85, 262, 569], Appl. 84/120, 397, 3pp. (1985). [Chem. Abst., 104, 167201u (1986)].

Nigam, S. K. and Mitra, C. R., Coloring matter of *Arnebia hispidissima*. *Indian J. Appl. Chem.*, **27**, 34-36 (1964).

Papageorgiou, V. P., Pharmaceutical composition for treating *Ulcus cruris*. *Ger. Offen.* 2, 700, 448, Appl. Jan. 1977, 11pp. (1978). [Chem. Abst., 89, 152707m (1978)].

Papageorgiou, V. P., Naturally occuring isohexenylnaphthazarin pigment: A new class of drugs. *Planta Medica*, **38**, 193-203 (1980).

Papageorgiou, V. P., Liakopoulou-Kyriakides, M. and Papadakie, C., Quantitative determination of isohexenylnaphthazarin pidgments by TLC densitometry. *Flovour Fragrance* J., **1**(1), 21-24 (1985). [Chem. Abst., 105, 72m (1986)].

Papageorgiou, V. P., Mellidis, A. S. and Sagredes, A. N., Study on the antibiotic fraction of *Alkanna tinctoria* Tausch. *Chem. Chron* **9**, 57-63 (1980). [Chem. Abst., 94, 25645t (1981)].

Pimenova, M. E. and Tareeva, N. V., Varition of shikonin content in subterranean organs of *Macrotomia euchroma*. *Rastit Resur* 16(1), 82-86 (1980). [Chem. Abst., 92, 143310m (1980)].

Romanova, A. S., Ban Kovskii, A. I. and Boryaev, K. I., Extration of shikonin. *All Union Scientific Research Institute of Medicinal and Aromatic plants, U.S.S.R.* 200, 737 (Cl. A. 61 K) Aug. 15, 1967, Appl. Oct. 7, 1966 (1966). [Chem. Abst., 68, 62965t (1968)].

Romanova, A. S., Ban Kovskii, A.I., Tareeva, N. V., Boryaev, K. J. and Gubanov, I. A., Shikonin. U.S. S.R. 240, 933 (Cl. A61 K) Appl. 15 Apr. 1968, From *Otkytiya Izobret, Prom. Obraztsy, Tovarnye*

Znaki, 46(13), 73 (1969). [Chem. Abst., 71, 53591r (1969)].

Romanova, A. S., Tareeva, N. V. and Ban Kovskii, A. I., Isolation of shikonin from *Onosma caucasicum* and *Echium rubrum*. *Khim. Prir. Soedin*, **3**(1), 71 (1967). [Chem. Abst., 67, 18548c (1967)].

Romanova, A. S., Tareeva, N. V., Pervykh, L. S., Kalashnikoa, G. K., Boryaev, K. I., Pakalans, D. and Patudin, A. V., Shikonin from *Macrotomia echiodies, Onosma livanovii, O. sericeum* and *O. setosum*. *Khim. Prir. Soedin*, 1, 96 (1981). [Chem. Abst., 95, 3375y (1981)].

Rukuzin, M. A. and Pekarsakava, G. F. Adsorption of alkannin from differnet solvents *J. Russ. Phys. Chem. Soc.*, 48, 716-718 (1916). [Chem. Abst., 11, 781^{9} (1917)].

Sankawa, U., Ebizuka, Y., Miyazaki, T., Isomura, Y., Otsuka, H., Shibata, S., Inomata, M. and Fukuoka, F., Antitumor activity of shikonin and its derivatives. *Chem. Pharm. Bull.*, **25**(9), 2392-2395 (1977).

Sankawa, U., Otsuka, H., Kataoka, Y., Iitika, Y. Hoshi, A. and Kuretani, K., Antitumor activity of shikonin, alkannin and their derivatives II. X-ray analysis of cycloalkannin leucoacetate, Tautomerism of alkannin and cycloalkannin and leucoacetate, and antitumor activity of alkannin derivatives. *Chem. Pharm. Bull.*, **29**(1), 116-122 (1981).

Seshadri, C., Nisteshwar, K., Venkataranghavan, S. and Venkataraman, S., Antifungal activity of *Alkanna tinctoria* (Diveshvalli). *Nagarjun*, **29**, 1-2 (1985).

Shcherbanovskii, L. R. *Onosma visianii* as a new shikonin source. *Khim. Prir. Soedin* (4), 517-518 (1971). [Chem Abst. 76, 56612n (1972)].

Shcherbanovskii, L. R. Shikonin from *Onosma tauricum*. *Khim. Prir. Soedin*, (2), 238 (1972a). [Chem. Abst., 77, 58848p (1972)].

Shcherbanovskii, L. R. Shikonin from *Onosma polyphy11um*. *Khim. Prir. Soedin*, (5), 666 (1972b). [Chem. Abst., 78, 108224a (1973)].

Shcherbanovskii, L. R. and Luks, Yu. A., Shikonin from *Echium lycopsis*. *Khim. Prir. Soedin*, (4) 513-514 (1974). [Chem. Abst., 82, 28587p (1974)].

Sherbanivs' kii, L. P. Presence of shikonin in some species of the family Boraginaceae, and its effect on lactic acid bacteria. *Ukr. Bot. Zh.*, **28**, 504-508 (1971). [Chem. Abst., 76, 68687d (1972)].

Shukla, Y. N. Tondon, J. S., Bhakuni, D. S. and Dhar, M. M., Chemical constituents of the antibiotic fraction of *Arnebia nobilis*. *Experientia*, **25**, 357-358 (1969).

Shukla, Y. N., Tondon, J. S., Bhakuni, D. S. and Dhar, M. M., Naphthaquinones of *Arnebia nobilis*. *Phytochem.* **10**(8), 1909-1915 (1971).

Sung, Chin-Wen, Liu, Kuo-Sheng and Li, Nai-Wen, Survey on Resource of *Lithospermum erythrorhizon* and related herbs in China. *Yao Hsuch Tung Pao*, **15**(5) 3-5, (1980). [Chem. Abst., 94, 71295b (1981)].

Tabata, M. and Honda, Y. Tropical bactericides containing deoxyshikonin. *Jpn. Kokai tokkyo Koho JP* 62, 289, 516 (87, 289, 516), Appl. 86/131, 792, 4pp. (1987). [Chem. Abst., 109, p 806m (1988)].

Tareeva, N. V., Romanova, A. S. and Ban Kovskii, A. I., Detection of shikonin in Boraginaceae plants. *Sb. Nauch. Rab. Ves. Nauch. Isslad. Ist. Lek. Rast.* (11), 175-178 (1970). [Chem. Abst., 76, 70042h, (1972)].

Tsukada, M., Fukui, H., Habara, C. and Tabata, M., Comparative studies on naphthaquinone derivatives in various crude drugs of 'Zicao' (Shikon). *Shoyakugaku Zasshi*, **37**, 299-306. (1983).

Tsukada., N. A., Fukui, H. and Tabata, M., Abstracts of papers 100th Annual meeting of the Pharmaceutical society of Japan, Tokyo, April, 1980, p.249.

Verma, M. R. and Dass, R., Acid base indicator from Ratanjot root. *Chemist Analyst*, **48**, 12-18 (1959).

Wilczek, E. Schweiz, Two new plants containing alkannin. *Apoth. Ztg. Suppl.* 14. (1924). [Chem. Abst., 19, 2108^{5} (1925)].

Xiang, Gui-uing, Lu, Fusun, Zhu, Fengchi, Li, Guofeng, Ye, Hechum, Dong, Jiaowang, Wu, Xin and Chen, Jian-Lin, Chemical Components of cell cultures of *Arnebia euchroma*. *Zhiwu Xuebao*, 34, 470-474 (1992). [Chem. Abst., 118, 98068f (1993)].

Xue, W. and Xu, D., Extraction and physicochemical properties of shikonin. *Shipin Kexue* (Beijing), 125, 25-28 (1990). [Chem. Abst., 113, 229889w (1990)].

Yoshizaki, F. and Hisamichi, S., Changes in shikonin derivatives contents during preserving of *Lithospermum* roots. Annu. Rep. Tohoku Coll. Pharm., 30, 61-64 (1983). [Chem. Abst., 98, 122808p (1983)].

Zhang, Min, Jin, Yongquing, Guo, Lanjian and Cai, Yujing, Shikonin in *Arnebia euchroma* and *Lithospermum erythrorhizon*. *Zhongeaoyao*, **20**,

449-450 (1989). [Chem. Abst., 112, 33368k (1990)].

Zhu. F., Lu, F. and Xing, G., Isolation of shikonin and its derivatives by HPLC. *Sepu*, **1**(2), 13 (1984). [Chem. Abst., 103, 59142w (1985)].

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