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Biodiversity in the Alkaloids of Annual *Papaver* Species of Turkish Origin

Türkiye'de Yetişen Tek Yıllık *Papaver* Türlerinin Alkaloitlerinde Biyodiversite

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Abstract

Eight annual Turkish *Papaver* species from sections Argemonidium (*P.argemone*), Carinatae (*P.macrostomum*), Mecones (*P.gracile*) and Rhoeadium, (*P. commutatum* subsp. *euxinum*, *P.dubium* subsp.*dubium*, subsp.*laevigatum*, subsp.*lecoqii*, *P.lacerum*, *P.rhoeas*, *P. rhopalothece*) have been investigated for their alkaloid contents. Presence of proaporphine type (1), mecambrine, pronuciferine, aporphine type (2), corydine, dehydroroemerine, isocorydine, N-methylasimilobine, roemerine, roemerine N-oxyde, rhopalotine, protopine type (3), allocryptopine, coulteropine, cryptopine, protopine, isopavine type (4), amurensine, amurensinine, protoberberine type (5), berberine, cheilantifoline, coptisine, sinactine, stylopine, tetrahydropseudocoptisine, thalifendine, phthalideisoquinoline type (6), narcotine, narceine, cularine type (7), cularine, spirobenzylisoquinoline type (8), fumariline, fumarophycine, rhoeadine type (9), isorhoeadine, papaverrubine A, rhoeadine, rhoeagenine, have been shown in the species. The existence of isopavine, phthalideisoquinoline, spirobenzylisoquinoline and cularine types have been shown for the first time in the sections studied.

Key words: Papaveraceae, annual *Papaver*, biodiversity, alkaloid.

Introduction

In Flora of Turkey, annual *Papaver* species are grouped into 4 sections, namely, Argemonidium, Carinatae, Mecones and Rhoeadium by Cullen (Cullen 1965). Recently Kadereit has revised some sections of genus *Papaver* in detail (Kadereit 1986, 1988). According to Cullen and Kadereit the acceptance of the species in the sections Argemonidium and Rhoeadium differ as follows.

Section Argemonidium Spach (Syn. Argemonorhoeades Fedde)

Cullen 1965	Kadereit 1986
P. argemone L.	*P. argemone* L. subsp.*davisii* Kadereit
P. hybridum L.	subsp. *minus* (Boiss.) Kadereit
P. virchowii Aschers & Sin. ex Boiss.	subsp.*nigrotinctum*(Fedde) Kadereit

Section Rhoeadium Spach (Syn.Orthorhoeades Fedde)

Cullen 1965	*Kadereit 1988*
P. arenarium Bieb.	*P. arachnoideum* Kadereit
P. clavatum Boiss.& Hausskn.ex Boiss.	*P. arenarium* M.Bieb
P. commutatum Fisher & Meyer	*P. clavatum* Boiss.& Hausskn.ex Boiss.
P. dubium L.	*P. commutatum* Fisher & C.Meyer
P. lacerum Popov	subsp. *euxinum* Kadereit
P. postii Fedde	*P. dubium* L. subsp. *dubium*
P. rhoeas L.	subsp. *laevigatum(syn.: P. lacerum* Popov*)*
P. rhopalothece Stapf.	subsp. *lecoqii* (Lamotte) Syme
P. stylatum Boiss.& Bal.	*P.guerlekense* Stapf. (syn.: *P. rhopalothece* Staph)
P. syriacum Boiss.&Blanche ex.Boiss.	*P. purpureomarginatum* Kadereit
	P. rhoeas L.
	P. stylatum Boiss.& Bal.

Section Carinatae Fedde
This section is represented by only one species named as P. *macrostomum* Boiss. & Huet ex Boiss. by Cullen.

Section Mecones Bernh.
Cullen reported the existence of the following species in Turkey:
P. glaucum Boiss. & Hausskn.
P. gracile Boiss.
P. somniferum L.
Among them section Rhoeadium is the richest in the number of species. With the exception of *Papaver somniferum*, opium poppy from section Mecones, all the species in these sections grow wild in Turkey. The alkaloids of some of the species have extensively been studied and the presence of some chemotypes containing medicinally important alkaloids has been shown (Sarıyar *et al.*,1981; Sarıyar *et al.*,1990; Atay *et al.*,1996; Mat *et al.*, 2000; Kalav *et al.*,1989; Sarıyar 2002). It has also been observed that some species have been used as folk medicine as well as vegetable (Sarıyar *et al.*,1990). The alkaloid contents of annual *Papaver* species are relatively poor than the biennial or perennial ones. In this work the result of our investigations carried out on the alkaloids of annual Turkish *Papaver* species will be discussed from the point of their biodiversity.

Material and Method

Collection data for the samples investigated are given in table 1.

Table 1 - Samples of Turkish *Papaver* species avaible for extraction of alkaloids

Sample	Collection Data
Section Argemonidium	
P.argemone	Çanakkale, May 1989
Section Carinatae	
P.macrostomum	Zonguldak, June 1995
Section Mecones	
P.gracile	Denizli, May 1995
Section Rhoeadium	
P.commutatum subsp.*euxinum* I	Ordu, July 1994
P.commutatum subsp.*euxinum* II	Zonguldak, June 1995
P.dubium subsp.*dubium* I	Bolu, June 1995
P.dubium subsp.*dubium* II	Bolu, July 1997
P.dubium subsp.*laevigatum*	Denizli, May 1995
P.dubium subsp.*lecoqii*	Bolu, June 1995
P.lacerum	Kayseri, June 1977
P.rhoeas I	Muğla, May 1983
P.rhoeas II	Ordu, July 1995
P.rhopalothece	Muğla, May 1983

Extraction and isolation of alkaloids: Air dried powdered aerial parts were extracted by maceration in methanol. The filtered extract was concentrated to dryness under reduced pressure and the residue extracted with three successive quantities of 3 % sulphuric acid. The separated acidic extracts were combined, washed with light petroleum, made alkaline with ammonium hydroxide (25 %) and extracted with three successive quantities of chloroform. The combined chloroform extracts were washed with water, separated, dried over anhydrous sodium sulphate, filtered and evaporated to dryness under reduced pressure. Column chromatography and preparative thin laver chromatography have been used for the isolation of alkaloids (Mat *et al.*, 2000).

Identification of alkaloids: The alkaloids have been identified by comparing their physical and spectral data (mp, UV, IR, ^{1}H-NMR and mass spectrometry) and TLC Rf values with those of authentic samples.

Results and Discussion

The scientific literature on annual *Papaver* alkaloids is extensive as can be appreciated by reference to the three excellent review articles by Santavy 1970, 1979 and by Preininger 1986. The investigations on the alkaloids of annual Turkish *Papaver* species have been carried out for twenty years and the results obtained so far are shown in table 2.

Table 2- Alkaloids isolated from Turkish annual *Papaver* species.

Species	Alkaloids	
Argemonidium		
P.argemone	**Protopine (3)**	Protopine (3a)
	Spirobenzylisoquinoline(8)	Fumariline(8a), Fumarophycine(8b)
Carinatae		
P.macrostomum	**Aporphine (2)**	Isocorydine (2b)
	Isopavine (4)	Amurensine(4a), Amurensinine(4b)
Mecones		
P.gracile	**Aporphine (2)**	Roemerine(2c),Dehydroroemerine(2e), Roemerine N-oxyde(2d)
	Proaporphine (1)	Mecambrine(1a)
Rhoeadium		
P.commutatum subsp.*euxinum* I	**Aporphine (2)**	Isocorydine(2b)
	Rhoeadine (9)	Rhoeagenine(9b), Papaverrubine A(9d)
P.commutatum subsp.*euxinum* II	**Aporphine (2)**	Isocorydine(2b)
	Isopavine (4)	Amurensinine(4b)
	Protoberberine (5)	Cheilantifoline (5d)
P.dubium subsp.*dubium* I	**Aporphine (2)**	Isocorydine(2b)
	Protoberberine (5)	Berberine(5a), Thalifendine(5c), Stylopine(5f), Tetrahydropseudocoptisine(5g)
P.dubium subsp.*dubium* II	**Aporphine (2)**	Corydine(2a), Isocorydine(2b)
	Protoberberine (5)	Berberine(5a), Thalifendine(5c)
P.dubium subsp.*laevigatum*	**Aporphine (2)**	Roemerine (2c)
	Proaporphine (1)	Mecambrine(1a)
	Protopine (3)	Protopine(3a), Allocryptopine(3b)
P.dubium subsp.*lecoqii*	**Aporphine (2)**	Roemerine(2c)
	Protoberberine (5)	Berberine(5a)
P.lacerum	**Aporphine (2)**	Roemerine(2c), N-Methylasimilobine(2g),
	Proaporphine (1)	Mecambrine(1a), Pronuciferine(1b)
P.rhoeas I	**Aporphine (2)**	Roemerine(2c), Isocorydine(2b)
	Protopine (3)	Protopine(3a), Allocryptopine(3b), Coulteropine(3c)
	Protoberberine (5)	Berberine(5a), Coptisine(5b), Sinactine(5e)
	Rhoeadine (9)	Rhoeadine(9a), Rhoeagenine(9b)
P.rhoeas II	**Rhoeadine (9)**	Rhoeadine(9a), Isorhoeadine(9c), Papaverrubine A (9d)
P.rhopalothece	**Aporphine (2)**	Isocorydine(2b), Roemerine(2c), Rhopalotine(2f)
	Cularine (7)	Cularine (7a)
	Phtalideisoquinoline (6)	Narcotine(6a), Narceine(6b)
	Protopine (3)	Protopine(3a), Cryptopine(3d)
	Protoberberine (5)	Berberine(5a), Coptisine(5b)

Section Argemonidium : The only Turkish sample investigated for its alkaloids is *P.argemone* (Sarıyar 2002). Protopine (**3a**) has been isolated as the major alkaloid from the species collected at Çanakkale. The minor alkaloids were spirobenzylisoquinoline type (8) fumariline (**8a**) and fumarophycine (**8b**) (Table 2). This is the first report of the presence of spirobenzylisoquinoline type in genus *Papaver*.

Section Carinatae: One sample of *P.macrostomum* collected from Zonguldak yielded isocorydine (**2b**)(aporphine type **2**) as the major alkaloid and amurensine(**4a**) and amurensinine(**4b**) (isopavine type **4**) as minor ones (Table 2) (Sarıyar 2002). All these alkaloids have been isolated for the first time from a sample of *P.macrostomum*. Two samples collected from Malatya and Van are still under investigation. Chromatographic examinations (TLC) of the alkaloidal extracts of these samples have shown that they differ in their alkaloid contents. This result indicates the presence of several chemotypes in Turkey.

Section Mecones: Among three species *P. somniferum* , the most important sample of the genus *Papaver* containing medicinally important alkaloids morphine, codeine and papaverine has been cultivated in Anatolia since Hittites. The other two species grow wild. Four alkaloids have been isolated from *P. gracile* collected from Denizli. These alkaloids were aporphine type(**2**) roemerine(**2c**) (major alkaloid), dehydroroemerine(**2e**), romerine N-oxyde(**2d**) and proaporphine type (**1**) mecambrine(**1a**)(Table 2). There is only one previous report on the alkaloid content of the species indicating the presence of two alkaloids of benzophenanthridine type oxysanguinarine and rhoeadine type rhoeadine(**9a**) (Preininger 1986).

Section Rhoeadium: The species in this section, investigated for their alkaloid contents, are *P. commutatum* subsp. *euxinum* , *P.dubium* (subsp.*dubium*, subsp.*laevigatum*, subsp.*lecoqii*), *P.lacerum, P.rhoeas, P. rhopalothece.*

Two samples of *P. commutatum* subsp.*euxinum* collected from East Black Sea Region (Ordu) and West Black Sea Region (Zonguldak) have been investigated (Atay *et al.*,1996). Both samples yielded isocorydine(**2b**) as the major alkaloid but they differ in their minor alkaloid contents (Table 2) . Presence of isopavine (**4**) alkaloid has been shown for the first time in this section.

Three subspecies of *P.dubium* in Turkey are recognized by Kadereit: *P.dubium* subsp.*dubium*, subsp.*laevigatum* and subsp.*lecoqii*. Two samples of *P.dubium* subsp.*dubium* have been studied and the alkaloids obtained are given in table 2 . The existence of thalifendine (**5c**) has been shown for the first time in Papaveraceae. Previously it was found only in *Thalictrum* (Ranunculaceae) species. Tetrahydropseudocoptisine(**5g**) which was prepared semisynthetically from pseudocoptisine has been isolated as a new natural alkaloid during our investigations (Mat *et al.*, 2000). *P.dubium* subsp.*laevigatum* yielded roemerine(**2c**) as the major alkaloid. The similarities of the alkaloid contents between *P.dubium* subsp.*laevigatum* and *P.lacerum* (Sarıyar 1981) are significant since the latter has been accepted by Kadereit as a synonyme for *P.dubium* subsp.*laevigatum* .

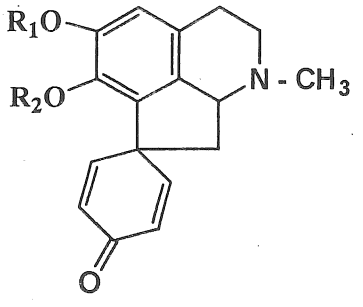
The most interesting species of the genus is *P. rhopalothece* which has now been named as *P. guerlekense* by Kadereit (Kadereit 1988). Two major alkaloids have been isolated, an aporphine type(**2**) isocorydine(**2b**) and phthalideisoquinoline type(**6**) narcotine(**6a**). Presence of narcotine as the major alkaloid in the species explains the traditional use of the plant as antitussive (Sarıyar *et al.*1990). Rhopalotine(**2f**) has been identified as a new aporphine

isolated from *P. rhopalothece* . The finding of cularine type(7) in a *Papaver* species is somewhat surprising since this type had previously been detected only in Fumariaceae.
Previous reports on the alkaloid content of *P.rhoeas* show the great variation within this species. Two samples of *P.rhoeas* both yielded rhoeadine(**9a**) as the major alkaloid (Kalav *et al.*,1989). A minor alkaloid protopine type(**3**) coulteropine(**3c**) was isolated for the first time from a *Papaver* species which was thought to be unique to the genus *Romneya* .
The types of the alkaloids found in annual *Papaver* species of Turkish origin are shown in table 3. Isopavine(**4**), phthalideisoquinoline(**6**), spirobenzylisoquinoline(**8**) types have been found in the sections for the first time.

Table 3- Types of alkaloids found in annual *Papaver* species of Turkish origin

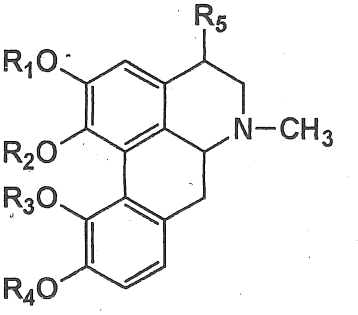
	Argemonidium	Carinatae	Mecones	Rhoeadium
Proaporphine (1)			+	+
Aporphine (2)		+	+	+
Protopine (3)	+			+
Isopavine (4)		+		+
Protoberberine (5)				+
Phthalideisoquinoline (6)				+
Cularine (7)				+
Spirobenzylisoquinoline (8)	+			
Rhoeadine (9)	+			+

Proaporphines (1)

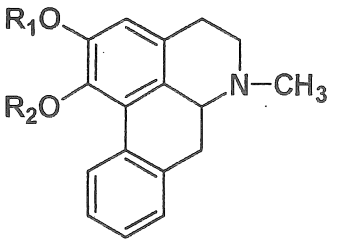


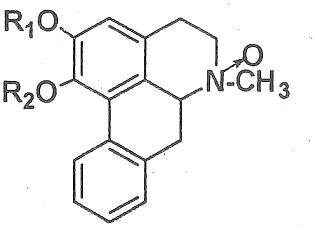
Mecambrine (1a) $R_1 + R_2 = CH_2$
Pronuciferine (1b) $R_1 = R_2 = CH_3$

Aporphines (2)



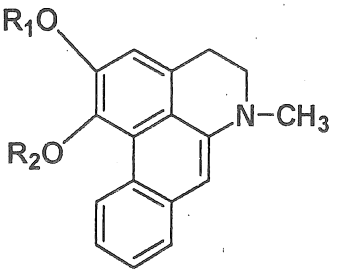
Corydine (2a) $R_1 = R_3 = R_4 = CH_3$, $R_2 = R_5 = H$
Isocorydine (2b) $R_1 = R_2 = R_4 = CH_3$, $R_3 = R_5 = H$
Rhopalotine (2f) $R_1 = R_2 = R_4 = CH_3$, $R_3 = H$, $R_5 = OH$





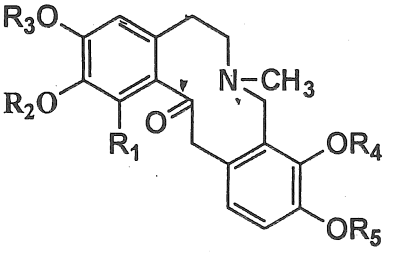
Roemerine (2c) $R_1 + R_2 = CH_2$ Roemerine N - oxyde (2d) $R_1 + R_2 = CH_2$

N-methylasimilobine (2g) $R_2 = CH_3$, $R_1 = H$



Dehydroroemerine (2e) $R_1 + R_2 = CH_2$

Protopines (3)



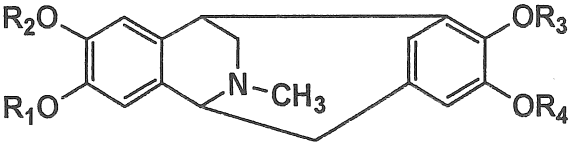
Protopine (3a) $R_1 = H$, $R_2 + R_3 = R_4 + R_5 = CH_2$

Allocryptopine (3b) $R_1 = H$, $R_2 + R_3 = CH_2$, $R_4 = R_5 = CH_3$

Coulteropine (3c) $R_1 = OCH_3$, $R_2 + R_3 = R_4 + R_5 = CH_2$

Cryptopine (3d) $R_1 = H$, $R_2 = R_3 = CH_3$, $R_4 + R_5 = CH_2$

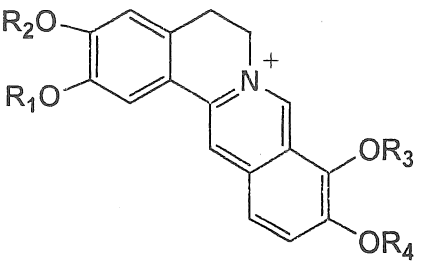
Isopavines (4)



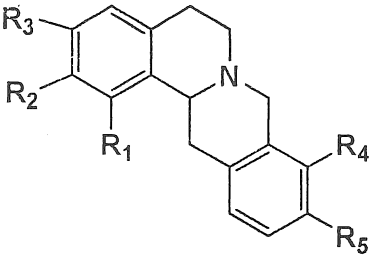
Amurensine (4a) $R_3 = CH_3$, $R_1 + R_2 = CH_2$, $R_4 = H$

Amurensinine (4b) $R_3 = R_4 = CH_3$, $R_1 + R_2 = CH_2$

Protoberberines (5)

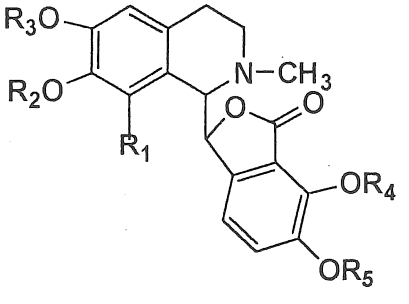


Berberine (5a) $R_1 + R_2 = CH_2$, $R_3 = R_4 = CH_3$
Coptisine (5b) $R_1 + R_2 = R_3 + R_4 = CH_2$
Thalifendine (5c) $R_1 + R_2 = CH_2$, $R_3 = CH_3$, $R_4 = H$

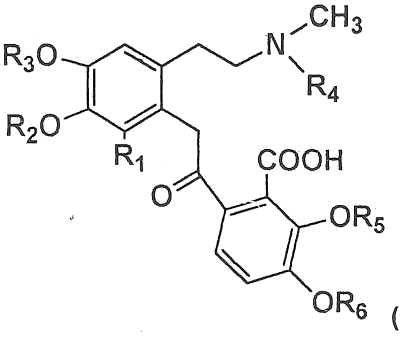


Tetrahydropseudocoptisine (5g) $R_1 + R_2 = OCH_2O$, $R_3 = H$, $R_4 + R_5 = OCH_2O$
Cheilanthifoline (5d) $R_1 = H$, $R_2 = OH$, $R_3 = OCH_3$, $R_4 + R_5 = OCH_2O$
Stylopine (5f) $R_1 = H$, $R_2 + R_3 = R_4 + R_5 = OCH_2O$
Sinactine (5e) $R_1 = H$, $R_2 = R_3 = OCH_3$, $R_4 + R_5 = OCH_2O$

Phtalideisoquinolines (6)



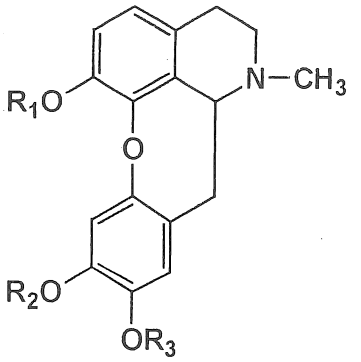
(a)



(b)

Narcotine (6a) $R_1 = OCH_3$, $R_2 + R_3 = CH_2$, $R_4 = R_5 = CH_3$
Narceine (6b) $R_1 = OCH_3$, $R_2 + R_3 = CH_2$, $R_4 = R_5 = R_6 = CH_3$

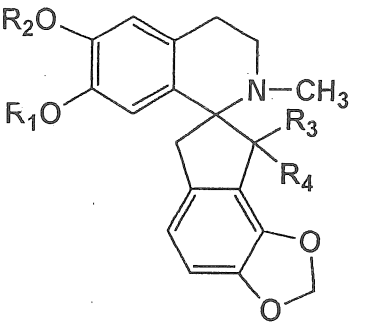
Cularines (7)



Cularine (7a) $R_1 = R_2 = R_3 = CH_3$

R_4=Acetyl

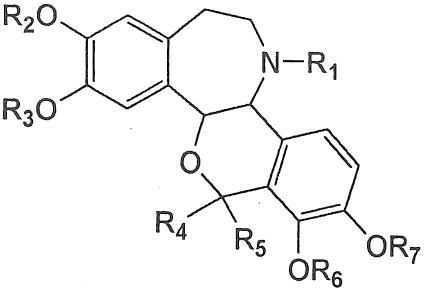
Spirobenzylisoquinolines (8)



Fumariline (8a) $R_1 + R_2 = CH_2$, $R_3 + R_4 = O$

Fumarophycine (8b) $R_1 = R_3 = H$, $R_2 = CH_3$,

Rhoeadines (9)



Rhoeadine (9a) $R_1 = CH_3$, $R_2 + R_3 = R_6 + R_7 = CH_2$, $R_4 = H$, $R_5 = OCH_3$

Rhoeagenine (9b) $R_1 = CH_3$, $R_2 + R_3 = R_6 + R_7 = CH_2$, $R_4 = H$, $R_5 = OH$

Isorhoeadine (9c) $R_1 = CH_3$, $R_2 + R_3 = R_6 + R_7 = CH_2$, $R_4 = H$, $R_5 = OCH_3$

Papaverrubine A (9d) $R_1 = R_4 = H$, $R_2 + R_3 = R_6 + R_7 = CH_2$, $R_5 = OCH_3$

Özet

Türkiye'de yetişen tek yıllık *Papaver* türlerinden Argemonidium (*P.argemone*), Carinatae (*P.macrostomum*), Mecones (*P.gracile*) ve Rhoeadium (*P. commutatum* subsp. *euxinum* , *P.dubium* subsp.*dubium*, subsp.*laevigatum*, subsp.*lecoqii*, *P.lacerum, P.rhoeas, P. rhopalothece*) seksiyonlarında yer alan 8 tür alkaloitleri açısından araştırıldı. Türlerde proaporphine(1) grubundan, mecambrine, pronuciferine, aporphine(2) grubundan, corydine, dehydroroemerine isocorydine, N-methylasimilobine, roemerine, , roemerine N-oxyde, rhopalotine, protopine(3) grubundan, allocryptopine, coulteropine, cryptopine, protopine, isopavine(4) grubundan, amurensine, amurensinine, protoberberine(5) grubundan, berberine, cheilantifoline, coptisine, sinactine, stylopine, tetrahydropseudocoptisine, thalifendine, phthalideisoquinoline(6) grubundan, narcotine, narceine, cularine(7) grubundan, cularine, spirobenzylisoquinoline(8) grubundan, fumariline, fumarophycine, rhoeadine(9) grubundan, isorhoeadine, papaverrubine A, rhoeadine, rhoeagenine alkaloitlerinin varlığı ortaya konuldu.

Çalışılan seksiyonlarda cularine, isopavine, phthalideisoquinoline ve spirobenzylisoquinoline gruplarına ait alkaloitlerin varlığı ilk kez bu çalışmada gösterildi.

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