

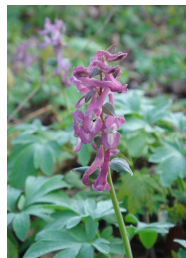
# Identification of Alkaloids from Fumariaceae Plants

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## Alkaloids – The Perfect Drug Leads?



**Corydalis cava L. (Fumarioideae), a source of isoquinoline alkaloids. Peissnitz island, Halle, April 2007.**

More than 15,000 naturally occurring alkaloids (mostly of herbal origin) have been found so far, and the number is increasing faster and faster. Although alkaloids often display unspecific biological activity, just this has not rarely turned out to be of therapeutic value. Even though only few genuine alkaloids are in use, many alkaloid derivatives are important as drug leads [1]. Frantz et al. have pointed out in a Nature News Feature 2005 called "Playing dirty" that it is quite reasonable not to use highly selective but "dirty drugs" for complex diseases, with a multi-target mechanism of action [2]. Finally the disappointing harvest of drugs from combinatorial chemistry underlines the advantage of a smart collection of natural products or derivatives thereof [3]. That is why natural products like alkaloids are very hopeful candidates when looking for lead substances.

In the following you will be introduced into common isoquinoline alkaloids of different classes and facile ways to quickly distinguish them from each other. Protopine, corydaline or bulbocapnine are the main alkaloids of Fumariaceae plants. Most of the alkaloids mentioned were isolated from Corydalis cava L. or Fumaria vaillantii Loisel. by J. Gadamer et al. at the beginning of the 20th century [4].

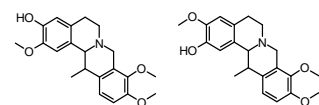
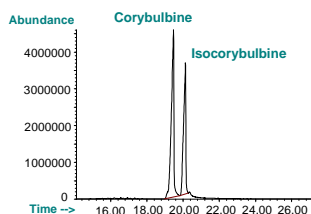
## GC-MS separation and identification of isoquinoline alkaloids

GC-MS: HP 5890 Series II  
Column: CP-Sil8CB/MS  
Method: 100 °C for 2 min.  
20 °C/min up to 280 °C  
hold for 20 min  
splitless injection

Alkaloid	Class	Retention time [min]
Cryptopine	PP	21.98
Protopine	PP	21.63
Alloccryptopine	PP	21.97
Corycavamine	PP	21.79
Corycavidine	PP	21.67
Canadine	PB	21.07
Corydaline	PB	19.89
Corybulbine	PB	20.01
Isocorybulbine	PB	20.63
Corypalmine	PB	21.69
Stylopine	PB	20.44
Tetrahydropalmatine	PB	21.69
Thalictricavine	PB	18.87
Scoulerine	PB	24.46
Adlumidine	PI	26.25
Parfumine	SBI	27.73
Bulbocapnine	AP	21.55
Corydine	AP	18.38
Isocorydine	AP	18.40
Nantenine	AP	17.50

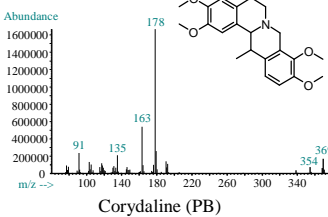
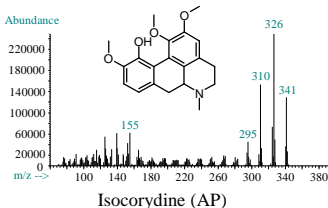
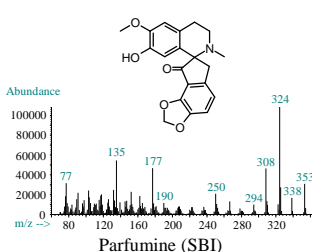
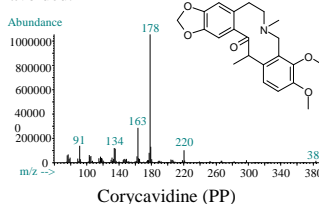
### Classes of isoquinoline alkaloids

PP – Protopine  
PB – Protoberberine  
PI – Phthalideisoquinoline  
SBI – Spirobenzylisoquinoline  
AP – Aporphine



Separation of the constitutional isomers, corybulbine (left) and isocorybulbine (right) by GC-MS. Differences in MS spectra are marginal in this case, but the HP ChemStation Software finds a match quality of approx. 95 %.

Due to structural resemblances of the alkaloids, overlap of peaks cannot be avoided.



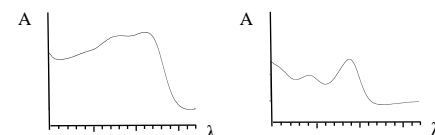
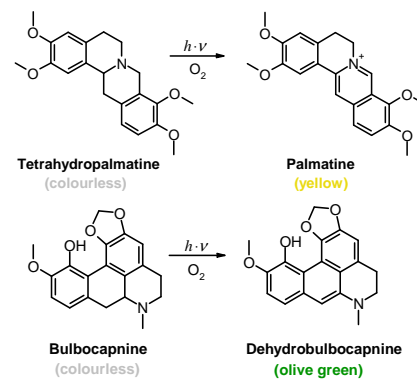
## TLC and UV data

Alkaloid separation was best using a ternary eluent system of ethylacetate:t-butylmethyl ether:toluene (4:3:1) with 5% conc. ammonia on Merck HPTLC plates Si 60 F<sub>254</sub>. UV-spectra were recorded in reflection mode on a Shimadzu TLC Scanner CS-930.

Alkaloid	R <sub>f</sub> value	Hue
Canadine	0.68	Yellow
Corydaline	0.71	Yellow
Corybulbine	0.74	Yellow
Isocorybulbine	0.72	Yellow
Corypalmine	0.44	Yellow
Stylopine	0.67	Yellow
Tetrahydropalmatine	0.67	Yellow
Thalictricavine	0.81	Yellow
Scoulerine	0.27	Brown
Bulbocapnine	0.55	Grey
Corydine	0.42	Grey
Isocorydine	0.36	Grey
Nantenine	0.57	Grey

Differentiation of protoberberine alkaloids by R<sub>f</sub> value and colour of the oxidation product is not easily possible, whereas aporphine alkaloids can be identified with certainty.

After development of the plates, aporphine and protoberberine alkaloids undergo quick oxidation esp. when exposed to direct sunlight. As a result, the alkaloids show typical colourful spots (see figure and table). The bathochrome shift supports the following reaction mechanism:

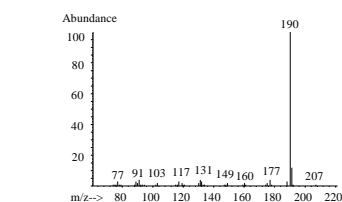


Typical shape of UV spectra for aporphine (left) and protopine alkaloids (right) from 200 to 400 nm

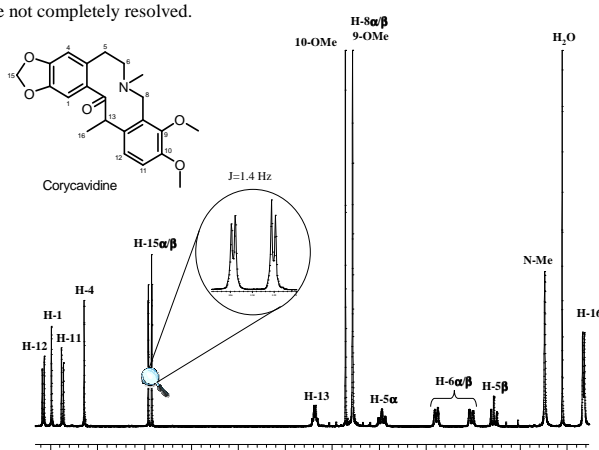
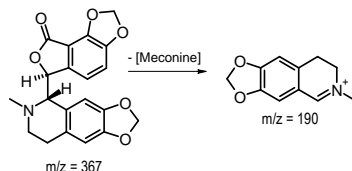
## Spectral analysis

Even on the basis of few MS data, a coarse structural determination is possible, of course lacking stereospecific information. NMR spectra of isoquinoline alkaloids display typical substitution patterns and reveal conformational preferences, but quite often aliphatic proton signals are not completely resolved.

For a protopine alkaloid, corycavidine has an unusually well resolved <sup>1</sup>H NMR spectrum due to the methyl group at C-13



Formation of main fragment of adlumidine (PI) after EI-MS



## Summary

Isoquinoline alkaloids offer a variety of chemical structures. For coarse and quick structure determination, GC-MS is the method of choice [5]. TLC and UV data interpretation require reference or archive data but are still useful for proximity screens. NMR data do not necessarily lay open the molecular constitution, but contribute to structure elucidation. A skilful analyst with some analytical experience is indispensable.

## References

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