SCREENING FOR *IN VITRO* ANTIFUNGAL ACTIVITIES OF SOME INDOLE ALKALOIDS

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In the course of investigations of the biological properties of indole alkaloids extracted from tropical *Strychnos* species, we realized a screening to detect if some of them displayed antifungal properties. The chosen alkaloids belong to the different skeleton types available in sufficient amount in our laboratory : tertiary or quaternary, substituted or unsubstituted, monomeric or dimeric, indole or indoline derivatives.
The minimum inhibitory concentration (MIC) was determined by the agar dilution technique on a panel of human pathogenic fungi, yeasts as well as dermatophytes. The maximum tested concentration was 100 µg/ml.
Our results indicate that the more active substances possess a β-carboline skeleton with an aromatic C ring. Hydrogenation of the 3-4 double bond drastically decreases the activity. Among the other indole skeleton-types tested, we only detected a slowing down of the growth of two strains of yeast for dimeric substances (strychnobiline and alloferine®). Our screening also indicates that antifungal activities are not linked with the cytotoxic, antimicrobial or antiparasitic properties. For example, some quasi-dimeric alkaloids possessing an usambarane skeleton have been shown to diplay antimicrobial, cytototoxic and/or antiparasitic acivities, but we did not find any activity against fungi.

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CALYSTEGINES, NOVEL GLYCOSIDASE INHIBITORS FROM *SOLANUM ELAEAGNIFOLIUM*

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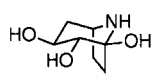
Calystegines are novel alkaloids of the tropane family, isolated from the roots of *Calystegia sepium*, *Solanum* and *Datura* species[1]. Such calystegines are polyhydroxylated nortropanes that are potent inhibitors of glycosidases and may be responsible for neurological disorders in livestock. Calystegines may also be regarded as a special class of azasugars, as represented by calystegin A_3 (**1**) and B_2 (**2**).

We have extracted calystegines from the fruits of *Solanum elaeagnifolium* CaV. (Solanaceae), used as diuretic in traditional Moroccan medicine, with ethanol (75%). The extract was subsequently purified by ion exchange chromatography[2]. Several hydroxylated alkaloids, an epimer of calystegin B_2 and an unknown pentahydroxylated nortropane have been detected by GC-MS. TLC and column separation can be achieved on silica gel using very polar eluent systems, such as ethanol:ammonia (4:1). Identification by spectroscopic techniques is in progress.



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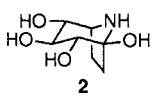

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BIOLOGICALLY ACTIVE CONSTITUENTS OF *CORDYCEPS SINENSIS*

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Cordyceps sinensis is a rare herb that has been used as traditional Chinese medicine for long. It is a dry complex composed of the sclerotium of the fungus *C. sinensis (Berk.) Sacc.* and the larva corpses of insects of *Hepialus armoricanus oberthur*, on which the fungus is parasitic[1]. Apart from exhibiting a number of specific medicinal properties, *C. sinensis* has gained worldwide reputation as Chinese long-distance race athletes allegedly take the herb along with other materials to build up their strength and to quickly recover after intense physical efforts[2].

According to the scarce literature in the field, nucleosides could contribute substantially to the biological activities of *C. sinensis*. Therefore, it was our aim to extract, separate and identify representative nucleosides. Method development included optimization of the extraction and separation conditions. After extraction with hot water, ion exchange chromatography, followed by macroreticular resin and TLC separation, led to appropriate fractionation of the extract. The collected fractions have been examined by spectroscopic techniques. Next to adenine and other nucleobases, a number of nucleosides appear to be present.

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HYPOGLYCEMIC ACTIVITY OF GALEGA OFFICINALIS

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Despite diet, oral antidiabetic agents and/or insulin, plants are frequently applied as adjuvants in the treatment of diabetes mellitus. This practice lacks pharmacological support. The aim of our work was to investigate the activity of 9 potential antidiabetic European plants.

Aqueous and ethanolic extracts were orally administered to male fasting Swiss mice (N=6 in each group), which were subjected at time 0 to an Oral Glucose Tolerance Test (OGTT, 5 g dextrose/kg bodyweight).
The aqueous extract of *Galega officinalis* (herb; 12,5 g dry crude material/kg bodyweight) almost completely suppressed the glucose peak. Decreases up to 66% at time 60 min were measured. At time 240 min, levels were still 30% lower as compared to the control group.

Galega did not lower an intravenously-induced hyperglycemia (1 g dextrose/kg bodyweight). Since the extract persistantly decreased the glycemia of fasting animals, both intestinal and metabolic effects can be presumed.

In order to purificate the complex water extract, samples were added to a cation-exchange column. Galegin, a guanidine derivative related to metformin, was retained by a SCX-column (Propylbenzenesulfonyl) and recovered in the acidic methanolic fraction. The presence of galegin was detected by TLC (Nitroprusside reagent, Rf=0,8).
Further studies to develop a (semi)preparative seperation technique and to investigate the mechanism of action are in progress.

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