

SECONDARY METABOLITES OF *PENICILLIUM* STRAINS FROM THE VKM SUBCOLLECTION OF EXTREMOTOLERANT FUNGI

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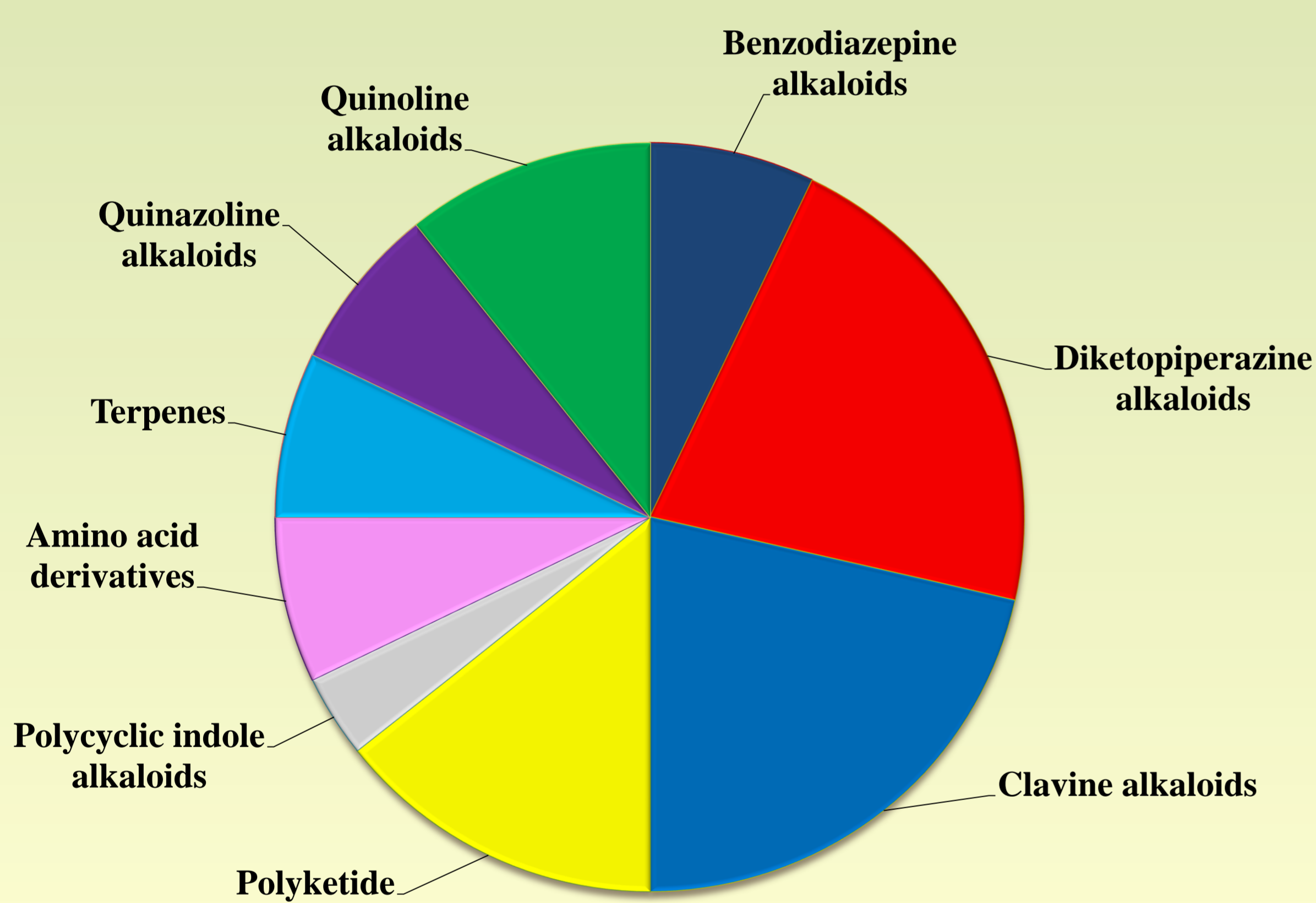
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In the low-temperature ecotopes a group of extreme-tolerant fungi highly adapted to the action of stresses have attracted attention. Fungi of the genus *Penicillium* have a special place among this group. These fungi are often found in the deep Arctic and Antarctic horizons, including the ancient ones dated back to millions of years. They also could be isolated from the surface deposits - both anthropogenically impacted and background sites. Approximately 900 fungal strains isolated from high latitude areas are maintained in All-Russian Collection of Microorganisms (VKM), 30% of them belong to the genus *Penicillium*.

The qualitative composition of secondary metabolites, mainly mycotoxins, was analyzed in 99 strains of 22 species of this genus. The strains were isolated in low-temperature habitats (26 strains from Antarctica and 73 from the Arctic).

These strains produced 56 secondary metabolites in some chemical subclasses. The most of discovered compounds belong to diketopiperazine alkaloids and clavine alkaloids (21.4% both). Quinoline alkaloids presented 10.7%, benzodiazepine alkaloids, terpenes, amino acid derivatives and quinazoline alkaloids – 7.1% each. Some secondary metabolites are of a group of polycyclic indole alkaloids (3.6%).



According to the practical needs of biotechnology a special database in had been constructed. The database contains information on secondary metabolites that are promising for biotechnology and are produced by *Penicillium* fungi. The database is a periodically updated information tool that provides researchers of various specializations with information about the biotechnological properties of fungal strains.

The database contains tables Metabolite and Biblio, built in a non-standard way and allowing you to quickly process the collected data and update the existing ones.

The Metabolite table has 15 fields, which contain information on the names of metabolites produced, including the class of compounds (in Russian and English); information about strain-producer: name (genus, species), strain number in the collections of the world.

The Biblio table contains 32 fields, including a complete bibliographic description of references pertaining to different types of publications - articles in journals, chapters in books, monographs, author's abstracts, patents, etc.

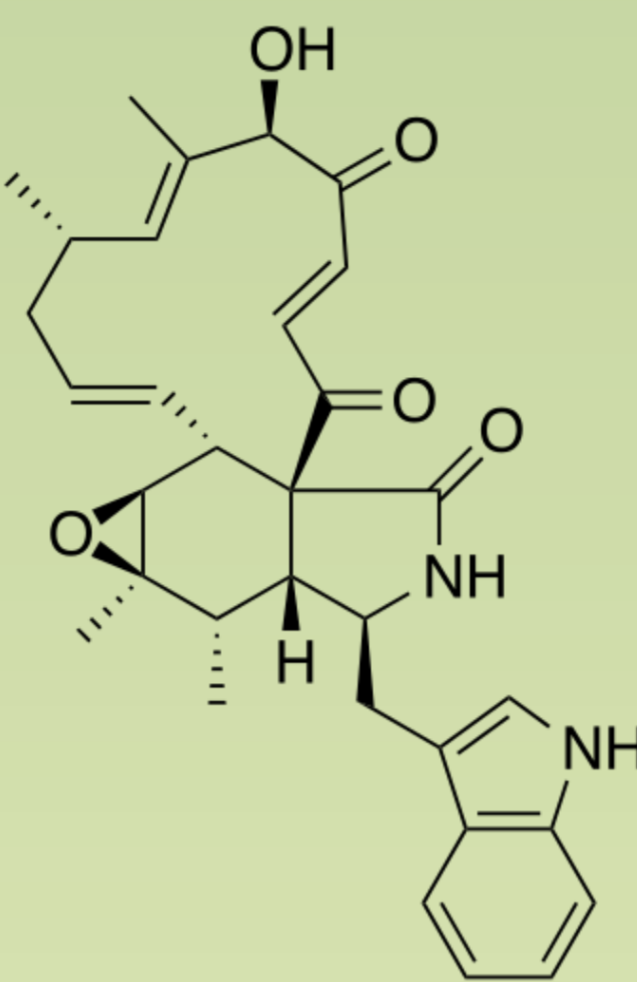
A special database had been presented in Internet. The database show the latest data on VKM fungal strains as well as the secondary metabolites produced. Appropriate links to StrainInfo (www.straininfo.net) were used to connect these data to the same strains in other microbial collections. More detailed control of fungal transfer between collections were inspected with the HISTRI links. Now, after the end of StrainInfo and HISTRI lifespan the lack of these tools is irretrievable.

References

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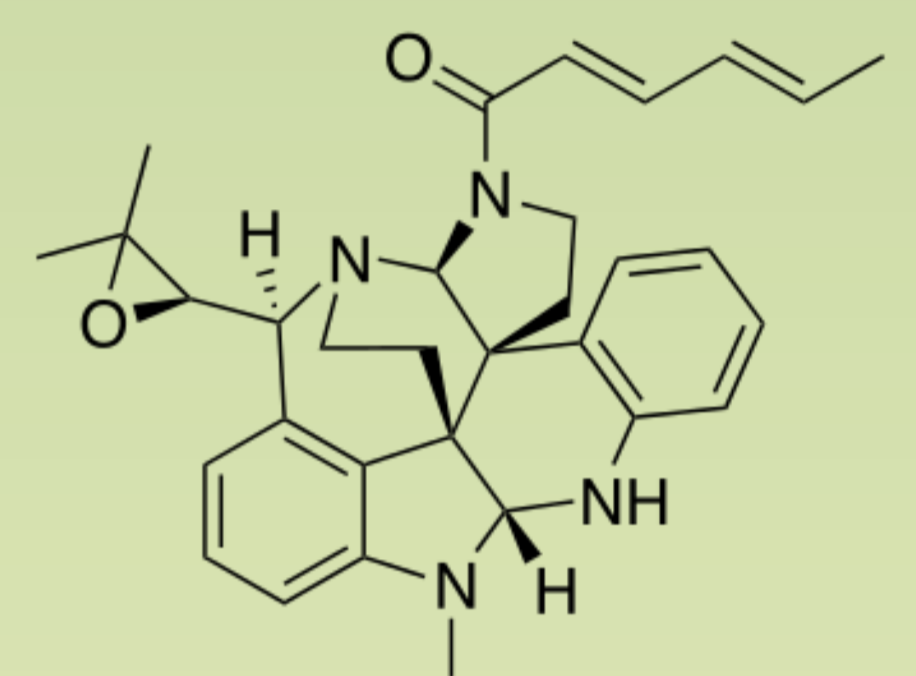
Along with the often allocated secondary metabolites, such as chrysogin and roquefortine, which occurred in 22% and 29% of the strains studied respectively, rare metabolites were detected, the practical value of which is quite high.

For example, strain *P. expansum* VKM F-4798 isolated from soil at Antarctic Bellingshausen station produced polycyclic indole alkaloids – communesin B and chaetoglobosin A.



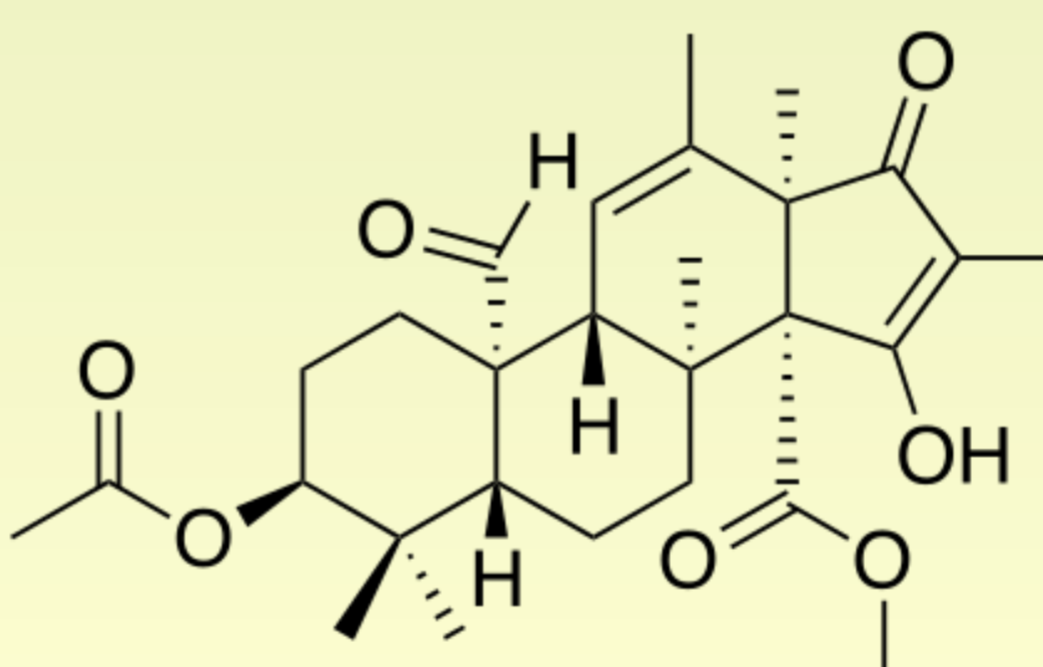
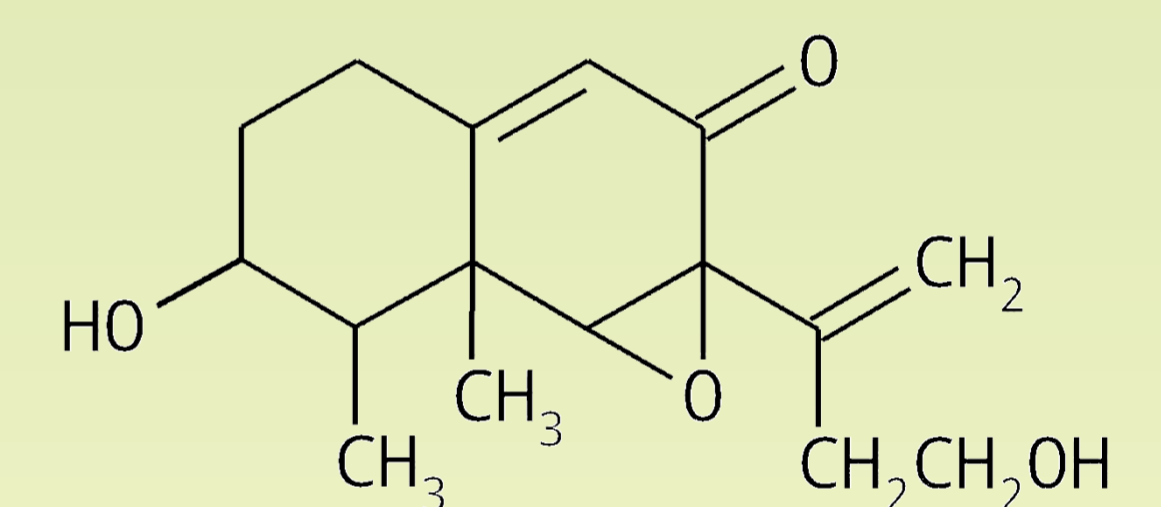
Communesin B exhibits a cytotoxicity with respect to various cell lines, anthelmintic and insecticidal activities (Kerzaon et al. 2009).

Chaetoglobosin A shows antibacterial, antifungal and antitumor activities, as well as phytotoxicity that can be used for developing novel herbicides (Jiang et al., 2017). Chaetoglobosins are intrinsic in nature to endophyte fungi and can play for them a defensive role by inhibiting other invasive fungi, by providing more life space to producers, that is they can accompany the stress states of the organism.



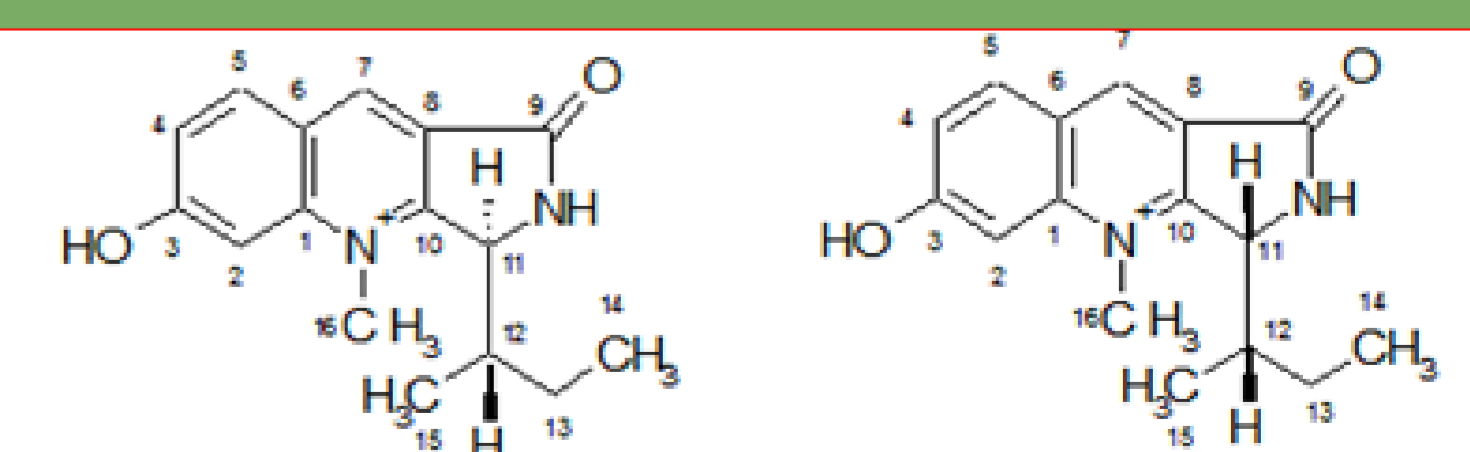
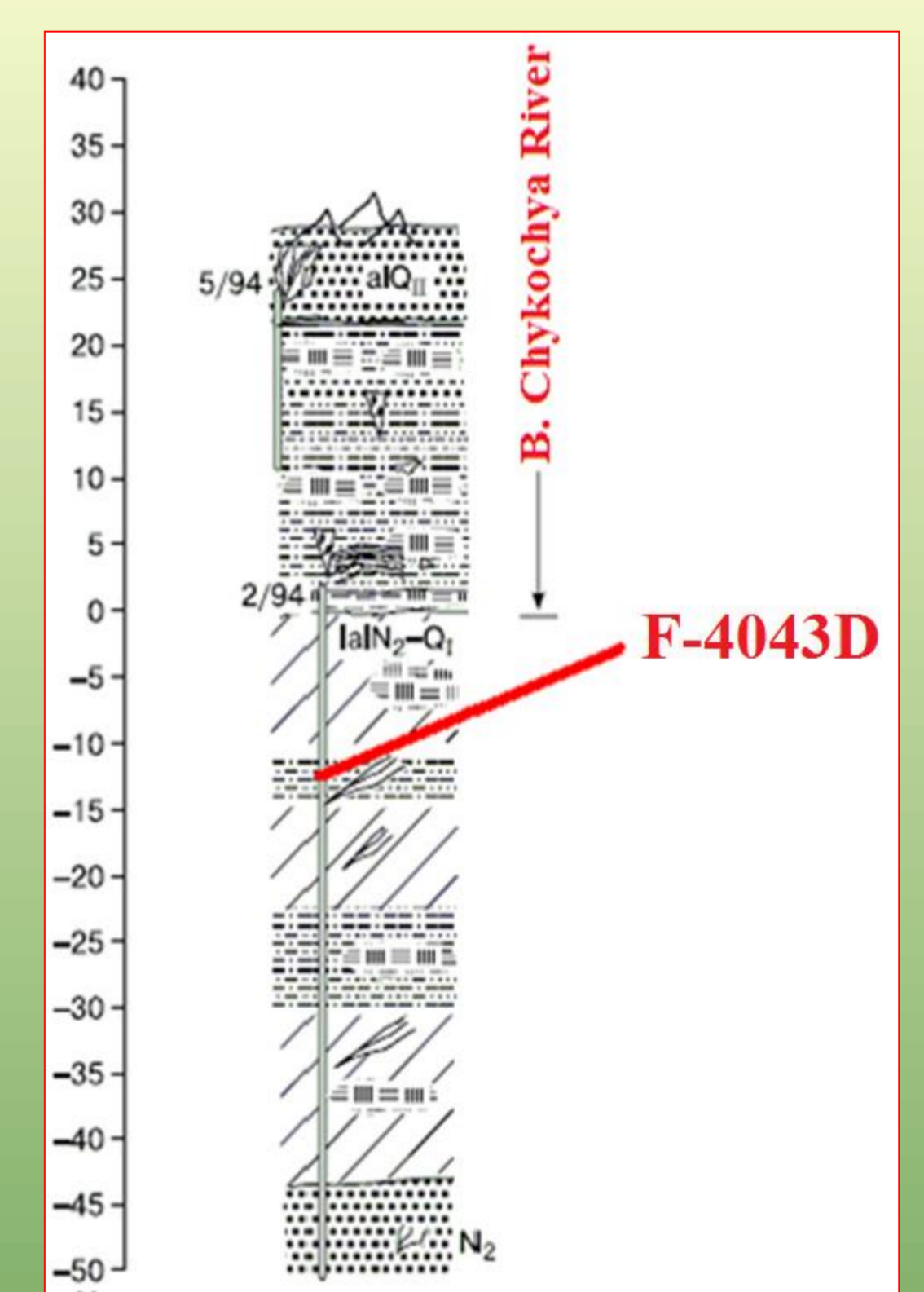
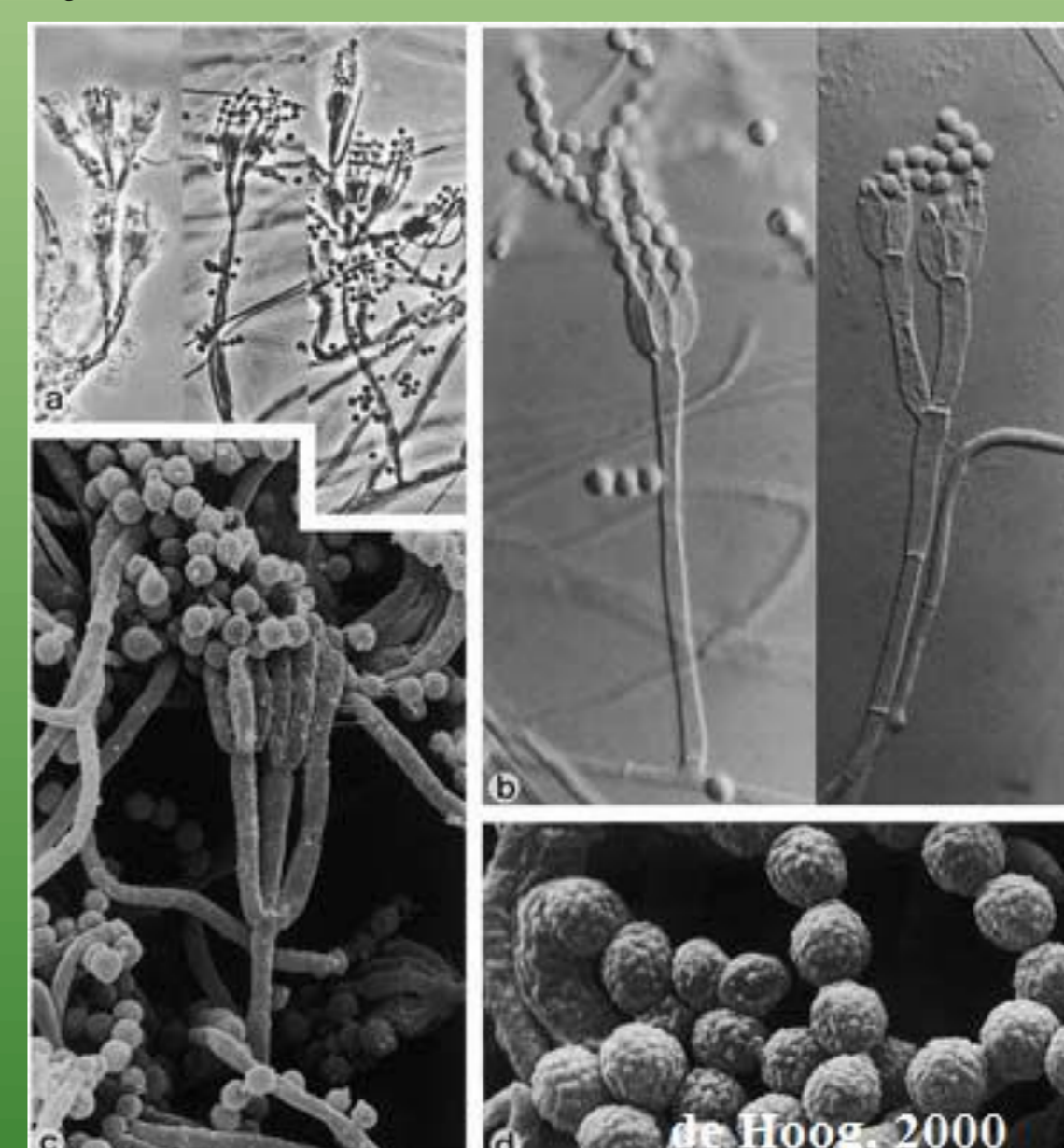
Strain *P. restrictum* VKM F-4796 was first found to produce terpenoids phomenon and andrastins A and C. This strain was found at the Antarctic research station Druzhnaya-4 in the place of petrochemical spill.

Phomenon efficiently inhibited the germination of seeds in many plants. This metabolite is an active inhibitor of RNA polymerase and, therewith, an inhibitor of protein synthesis at the stage of initiation and elongation (Silva et al. 2010).



Andrastin A possesses useful biological properties that make it promising for medicine, inasmuch as it contributes to the intracellular accumulation of anticancer compounds in tumour cells (Rojas-Aedo et al. 2017). The function of andrastin in the metabolism of the producing fungus is hard to establish; however, it is suggested to be involved in the regulation of the sterile profile of the organism, in particular, in the conversion of testosterone to 5 α -dihydrotestosterone, and the change in the lipid composition of the cell is the most widespread reaction to the action of stressors.

The strain of *Penicillium citrinum* VKM F-4043D, isolated from permafrost sediments of the Kolyma lowland, having an age of 1.8-3.0 Ma, formed novel quinoline alkaloids, which were named quinocitrinine A and quinocitrinine B. A study of the activity of these compounds on pro- and eukaryotic microorganisms showed that they have broad biological activity against gram-positive and gram-negative bacteria, yeasts and fungi. These metabolites were also cytotoxic for tumor cells.



Quinocitrinine A

Quinocitrinine B