Abstract: Four new lignans were isolated from *Haplophyllum pilosyulum*, their structures were established by spectral data, using COSY, HETCOR, COLOC, selective INEPT experiments. Pharmacological tests were performed on human cell lines and HIV-1 reverse transcriptase.

The success of semisynthetic anticancer drugs etoposide (1) and teniposide (2) focused the attention on the availability of podophyllotoxin (3) which was first isolated from *Podophyllum peltatum* L. later in higher quantity from *P.hexandrum* [1]. Since the total synthesis of podophyllotoxin is uneconomic, either systematic cultivation of the plant or tissue culture methods could be used to produce compound 3, a third way is to screen seed bearing plants for aryltetraline lignans [2]. During the
screening of this type plants, arylnaphtalene lignans were also found to possess antitumor activity. Since antitumor active arylnaphtalene lignans were isolated from *Haplophyllum* species together with diarylbutyrolactone lignans, this group of plants were also investigated. Among these plants *H.tuberculatum* yielded justicin A, B, diphyllin and tuberculatin [3], as well as antibacterial and antimitotic compounds polygamain and kusunokinin [4]. From *H.myrtifolium* two new lignans, an arylnaphtalene type, haplomyrtin and a diarylbutyrolactone type, (-)-haplomyrforlin were isolated [5]. *H.cappadocicum* revealed the presence of justicin A, B, diphyllin, 4-deoxyisodiphyllin, daurinol and isodaurinol [6]. Daurinol derivatives, daurinol glucoside and mono-O-acetyl/daurinol glucoside were found in *H.buxbaumii* [7]. Our studies with *Haplophyllum* species showed the presence of antitumor active lignans, justicin B (4) from *H.buxbaumii* [8], diphyllin (5) and a new compound 4-acetyl-diphyllin (6) from *H.telephioides* [9]. From *H.pilostylum* we have obtained compound 4 together with isodaurinol (7) [10], as well as arylbutyrolactone lignans, matairesinol (8) and arctigenin (9) [11].

In recent studies with the same extracts of *H.pillostylum* four new compounds were isolated. One of them was a new isomer of polygamain (1β-polygamain) (10), the other three were arylbutyrolactone lignans.
type lignans (11-13). The structures were established by using $^1$H NMR, $^{13}$C NMR and various techniques such as COSY, HETCOR, COLOC, DEPT and selective INEPT experiments. Compound 11 was established as 4-[6",7"-dihydroxygeranoyl]-matairesinol. Compound 12 was found as a mixture of two isomers and could only be differentiated from the $^{13}$C NMR spectrum and selective INEPT experiments and they were found as two isomers of 4-isopentylhaplomyrfolin type A and type B. In compound 13 the lactone ring of matairesinol moiety was reduced to alcohol and it carries a geraniol side chain. Compound 13 was also a mixture of two isomers corresponding to type A and type B. The structure of 13 was established as 4-geranoyl-9-hydroxymateiresinol. The bioassay showed that neither of the compounds was cytotoxic against a lung carcinoma (LU-1), a hormon dependant human prostate and hormon dependant breast cancer cell lines, but some moderate activity (IC$_{50}$=111.7 µg/ml) was observed for compound 10 in the HIV-1 reverse transcriptase (p66/p51) assay. Additional cytotoxicity tests is under investigation.
REFERENCES