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学位授与の要件	博士の学位論文提出者 (学位規則第 5 条第 1 項該当)
学位論文の題目	Chemical and Biotechnological Studies of Hydrolyzable Tannins of Plants of <i>Tamarix</i> Species ( <i>Tamarix</i> 種植物の加水分解性タンニンに関する化学的および生物工学的研究)
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#### 学位論文内容の要旨

In the first part of this study, chemical and biological studies of hydrolyzable tannins of tamaricaceous plants, 12 new ellagitannins including eight dimers, nilotinins D1-D5 and D7-D9, and four monomers, nilotinins M1-M4, were isolated from an aq. acetone extract of air-dried leaves of *T. nilotica* collected at Egypt. In addition, seven known ellagitannin dimers, hirtellins A, B, C and F, isohirtellin C, tamarixinin A, nilotin D6, and eight known monomers, 1,3-di-*O*-galloyl-4,6-*O*-(*S*)-hexahydroxydiphenoyl- $\beta$ -D-glucose, remurins A and B, hippomanin A, gemin D, tellimagrandins I and II, and 1,2,6-tri-*O*-galloyl- $\beta$ -D-glucose, were isolated for the first time from this plant species. The known dimers nilotin D6 and isohirtellin C were isolated from a plant extract for the first time. Structures were elucidated based on spectroscopic analyses and chemical correlations with known compounds. On the basis of the results, reported spectroscopic assignments for hirtellins A and B, tamarixinin A and the macrocyclic tannins hirtellins C and F and isohirtellin C were revised. Unusual shifts in the NMR spectra of these tannins are also discussed in relation to their conformations. The  $^{13}\text{C}$  NMR spectroscopic data for hirtellins C and F, isohirtellin C, tamarixinin A, and remurins A and B are also reported for the first time.

Because cytotoxic drugs play a major role in cancer chemotherapy, major *T. nilotica* dimers, hirtellins A and B, and tamarixinin A, together with some related tannins, remurins A and B, nilotinins M4 and D8, with good abundance in the plant, were tested for their possible direct cytotoxic activity on human oral squamous cell carcinoma (HSC-2, HSC-3, and HSC-4) and promyelocytic leukemia (HL-60) cell lines compared with their effect on human oral normal cells (HGF, HPC, and HPLF). Among all of the tested tannins, hirtellin A and nilotin D8 showed potent cytotoxic effects and elevated TS values at the applied concentrations against all tested tumor cell lines.

In the other part of this study, biotechnological studies of hydrolyzable tannins of tamaricaceous plants, we established shoot cultures of *T. tetrandra* capable of producing monomeric-tetrameric ellagitannins common to tamaricaceous plants.

The effects of light, and certain medium constituents such as concentrations of inorganic elements and vitamins, sucrose, and  $\text{Cu}^{+2}$ , and the effect of different nitrogen source  $\text{NH}_4^+/\text{NO}_3^-$  ratio on growth and the ellagitannins production of the cultured tissues were examined. Growth and ellagitannin production of shoots cultured on LS liquid medium with the same sugar and hormone components were also tested. Shoots transferred to LS hormone-free medium promoted root development, and the regenerated plants could adapt on the ordinary soil and climate. HPLC assessment of individual ellagitannins content of different organs of the naturally growing *T. tetrandra* plant as well as the content of tannins in the leaf part at different seasons were also achieved.

## 論文審査結果の要旨

本論文では、エジプトの乾燥地帯を中心に広く分布するギョリュウ科 *Tamaricaceae* 植物の *Tamarix nilotica* から、既知の加水分解性タンニンに加えて、新規加水分解性タンニン 2 量体 nilotin D1 – D9、および新規単量体 nilotin M1 – M4 を単離し、これらの構造について論じるとともに、既報の物質のスペクトルの帰属の修正をも行っている。これらのうち 2 量体はいずれも、*m*-dehydrodigalloyl、*p*-dehydrodigalloyl、あるいは hellinoyl 基によって架橋されたギョリュウ科植物独特の構造を有しており、それらの中には nilotin D5 のように大環状構造を有するものも見出されている。

これらの化合物のうち、比較的高収量で得られたものについて cytotoxicity が検討された結果、単量体の remurin B、2 量体の hirtellin A および nilotin D8 に、cytotoxicity について腫瘍細胞に対し正常細胞に比べて良好な選択性が見られた。

そこで、hirtellin A を主な対象として、*Tamarix tetrandra* を使用し、組織培養による安定な生産条件の検討のため、シュート培養系を確立し、光、培地濃度、無機成分（窒素原となる  $\text{NO}_3^-/\text{NH}_4^+$  比、および  $\text{Cu}^{2+}$  濃度）、糖濃度等についてその影響を明らかにするとともに、液体培地系の確立、さらに再分化をも行った。

これらの知見は、博士の学位にふさわしいものとする。