

N-acetyltyramine from *Phyllophora crispa* (Hudson) P.S. Dixon and N-acetylphenylethylamine from *Gelidium crinale* (Hare ex Turner) Craillon

Phyllophora crispa (Hudson) P.S Dixon'dan N-asetiltiramin ve *Gelidium crinale* (Hare ex Turner) Craillon'dan N-asetilfeniletilamin

Aline Percot¹, Kasım Cemal Güven^{2*}, Veysel Aysel³, Hüseyin Erduğan³ and Tuncay Gezgin⁴

¹Université Paris 6, Laboratoire de Dynamique Interactions et Réactivité, CNRS- UMR 7075, 2 rue Henri Dunant, 94320 Thiais, France.

²Turkish Marine Research Foundation (TUDAV), PO Box 10, Beykoz, Istanbul, Turkey.

³Çanakkale Onsekiz Mart University, Faculty of Science and Arts, Biology Department, Çanakkale, Turkey.

⁴Prolab. Laboratuar Teknolojileri Ltd. Pendik, Istanbul, Turkey.

Abstract

In this work N-acetyltyramine and N-acetylphenylethylamine were identified by GC-MS for the first time in a marine algae, *Phyllophora crispa* and *Gelidium crinale* respectively.

In our earlier work hordenine was found in both algae. Tyramine and phenylethylamine appear as a precursor of hordenine in barley. Similarly to these findings we suggested that the present compounds are also precursor for hordenine in algae.

Keywords: N-acetyltyramine, N-acetylphenylethylamine, *Phyllophora crispa*, *Gelidium crinale*, GC-MS.

Introduction

N-acetyltyramine is an acetyl derivate of tyramine (4-hydroxyphenylethylamine). It is an important amine for chemical and pharmacological purposes. Tyramine was found in many plants but is rare in algae (Smith 1977). Tyramine was detected in the following algae: *Chondrus crispus*, *Polysiphonia urceolata*, *Laminaria saccharina* (Kneifel et al. 1977) and in the micro algae *Scenedesmus acutus* (Rolle et al. 1977). N- acetyltyramine was produced by many macroorganisms as: *Streptomyces alni* (Liu 2009), *Microbispora aerata* IMBAS- 11 A (Ivanova et al. 2003), *Mycobacterium tuberculosis* (Sakurai 1958), *Cyathobasis fruticulosa* (Larghi and Kaufman 2007) and terrestrial plants as: *Aristolochia cucurbitifolia* (Tian- Shung et al. 1999), *Stapelia hirsuta* (Shabana et al. 2006) and *Olea europea* (Conde 2008).

*Corresponding author: kcguyen@yahoo.com

The tyramine is a pharmacologically important compound. It stimulates the central nervous systems, causes vasoconstriction, increases heart rate and blood pressure and is also responsible for migraine. (McKenna 1995). N-Acetyltyramine is a neuropeptide (Paxon et al. 2005).

N-acetylphenylethylamine (ACPEA) [N-(2-phenylethylacetamide)] is an acetyl derivate of 2-phenylethylamine. It is a natural compound biosynthesized from the aminoacid phenylalanine by enzymatic decarboxylation. 2-phenylethylamine was isolated from terrestrial plants (West et al. 1974, Shabana et al. 2006), from microorganisms (Hamasaki et al. 1993) and from marine algae by Steiner and Hartmann (1968) and recently by Percot et al. (2009) in several red algae. 2-phenylethylamine is a pharmacological active compound. It is a neuromodulator and a neurotransmitter. Substituted phenylethylamines is a broad chemical group that includes hormones, stimulants, hallucinogens, entactogenes, anorectics, bronchodilators and antidepressants. Some of the more important phenylethylamines are tyramine, dopamine, adrenaline, ephedrine, hordenine etc. (Saavedra 1978, Hanna and Eyre 1979, Hamasaki et al. 1993, McKenna 1995, Tocher and Tocher 1996, Sabelli et al. 1996). Hordenine, a phenylethylamine derivate was obtained from the marine algae *Phyllophora crispera* (old name *Phyllophora nervosa*) (Güven et al. 1969, 1970, Percot et al. 2007) and from *Gelidium crinale* (Yalçın et al. 2007).

N-acetyl hordenine was isolated from terrestrial plant *Stapelia hirsuta* L. (Shabana et al. 2006).

Phenylethylamine alkaloids have a phenylethyl nucleus. The group includes simple phenylamine (tyramine, hordenine), catecholamine (dopamine, noradrenaline, adrenaline), simple tetrahydroisoquinoline (mescaline, anhalamine, anhalonine, anhanolidine), benzyloisoquinoline (papaverine), phthalimide isoquinoline (mescaline), phenethylisoquinoline (autumnaline, florumultin and kreysigine, tetrahydroisoquinoline (emetine, cephaline) and terpenoid tetrahydroisoquinoline (Scologanine, ipecoside) (Spencer 1970, Mc Corkindale 1977, Snieckus 1971, Smith 1977, Aniszewski 2007).

N-acetylphenylethylamine has effects on the dopaminergic nigrostriatal system and induces rotations ipsilateral to the side of the brain lesion (Barroso and Rodriguez 1996).

In this work for the first time N-acetyltyramine was identified in marine algae *Phyllophora crispera* and N-acetylphenylethylamine was identified in *Gelidium crinale*.

Materials and Methods

The algae collected were:

Phyllophora crispera in Soğanlıdere, Dardanelles, April 2007

Gelidium crinale in Şile, the Black Sea in September 2006.

The chemicals and solvents used were purchased from Merck (Darmstadt, Germany), sodium sulfate from BASF (Germany) and ethanol from Tekel (Istanbul, Turkey). Reference compounds N-Acetyltyramine was prepared from tyramine HCl (Sigma, USA).

The alga samples were air dried and ground. 5 g algal samples were extracted first with 300 ml ethanol (90 %) and then with the same volume of acetone under reflux for 4 h. The organic phase was distilled in rotary evaporator at 40 °C. The residue was taken with 20 ml distilled water, then acidified with 2 N sulfuric acid and shaken. The aqueous phase was separated, filtered then alkalized with ammonia solution (5%) and extracted with 30 ml dichloromethane (DCM). The organic phase was separated and dried over sodium sulphate anhydrous and distilled at 40 °C. The residue was dissolved in 1 ml ethyl acetate /methanol mixture (1:1 v/v) and injected to GC-MS.

N-acetyltyramine was prepared after neutralization of tyramine HCl with ammonia solution (2%) and extracted with diethylether. The organic phase was separated and dried over sodium sulfate anhydrous, filtered and distilled at 36 °C. The acetyl derivat was obtained with anhydric acetic acid.

GC-MS analysis: The sample was analyzed using gas chromatography-mass spectrometry (HP6890 Series GC System; Hewlett Packard) fitted with an electronic pressure control and mass selective detection (HP 5972A) (ionization energy, 70 eV; source temperature, 280°C), using a HP-PONA capillary column (50 m x 0.25 mm i.d., 0.25 µm film thickness). The chromatographic conditions were as follow: sample size 2 µl, injection port temperature 280 °C, configured for split injection; initial oven temperature 40 °C rising to 280 °C at 8 °C/min, final hold of 20 min. Helium was used as the carrier gas (1 ml/min).

N-acetyltyramine (I) and N-acetylphenylethylamine (II) were identified by comparison of mass spectra of GC-MS with library data and reference mass spectra for I.

Results

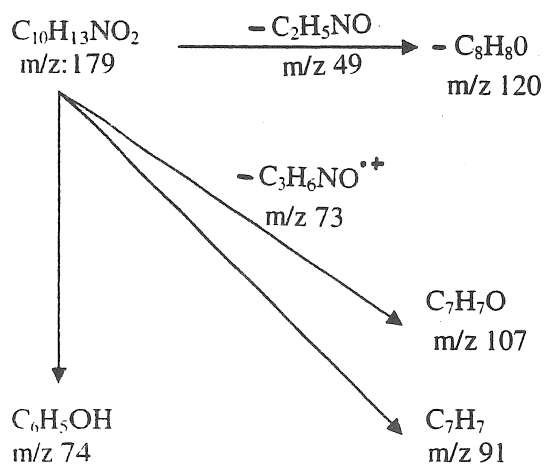
Mass spectra of N-acetyltyramine:

From *Phyllophora crispa* (m/z): 179, 120, 107, 94, 91

From HP memory: 179, 120, 107, 94, 91

From reference compound: 179, 120, 107, 94, 91

Mass spectral fragmentation of N-acetyltyramine.



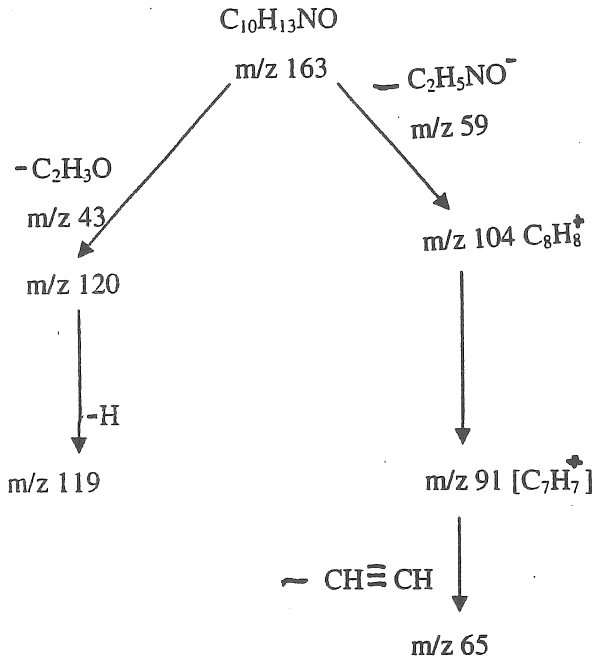
N-acetyltyramine was identified by comparison of its spectrum with library data and reference compound mass spectra.

MS spectrum of N-acetylphenylethylamine:

From *Gelidium crinale* (m/z): 163, 119, 104, 91, 65

From HP memory: 163, 119, 104, 91, 65

Mass spectral fragmentation of N-acetylphenylethylamine.



N-acetylphenylethylamine was identified by comparison of the mass spectra with library data of mass spectra.

Tyramine and phenylethylamine are important natural compounds for chemical and pharmacological field. Many alkaloids are produced from these substances. Its acetyl derivatives are also important. The status of tyramine and phenylethylamine are the subject of many studies on terrestrial plants (West et al. 1974, Shabana et al. 2006). 2- Phenylethylamine was found in algae (Percot et al. 2009). It is interesting for chemotaxonomical to point out the presence of N-acetyltyramine, N-acetylphenylethylamine and hordenine in the same algae.

We suggested that the compounds found in these algae are precursor of hordenine as in terrestrial plants (Marsicot and Mareon 1957).

Acknowledgment

This work was made in the laboratory of Institute of Marine Science and Management of University of Istanbul. The authors thank to Director Prof.Dr. E. Doğan for the support of this work.

Özet

Bu çalışmada deniz alglerinden *Phyllophora crista*'dan N-asetiltiramin ve *Gelidium cirinale*'den N-asetilfeniletilaminin tanımlanması gas-mass spektrofotometresiyle tanımlanmıştır. Tiramin kara bitkilerinde, mantarda, hayvansal ve bitkisel gıdalarda mevcuttur. Tiramin farmakolojik açıdan önemli bir maddedir. Hipertansif etkidedir. Migren ağrısına sebep olur. Feniletilamin bitkilerde ve alglerde bulunur, N-asetilfeniletilamin ise dopinerjik nigrostriyal sisteme etkilidir. Kimyasal açıdan tiramin ve 2-feniletilaminin bir alkaloid olup ve kara bitkilerinde bulunan hordeninin öncüsü olduğu kabul edilir. Hordenin'in deniz alglerinde bulunduğu ilk defa tarafımızdan bildirilmişti. Tiramin ve feniletilaminin kara bitkilerinde hordeninle bir bağıntısı olduğu bildirilmiştir. Bu çalışmada alglerde tespit edilen N-asetiltiramin ve N-asetilfeniletilamin'in hordenin ile bir bağıntısı olduğu düşünülmüştür.

References

- Aniszewski, T. (2007). *Alkaloids- Secrets of Life*, Elsevier, Amsterdam. p. 316
- Brasso, N. and Rodriguez, M. (1996). Action of β -phenylethylamine and related amines on nigrostriatal dopamine neurotransmission. *Europ. J. Pharmacology* 3: 195-203.
- Conde, E., Cara, C., Moure, A., Ruiz, E., Castro, E., Dominguez, H. (2009). Antioxidant activity of the phenolic compounds released by hydrothermal treatment of olive tree pruning. *Food chemistry* 114: 806-812.
- Güven, K.C., Bora, A. and Sunam, G. (1969). Alkaloid content of marine algae. I. Hordenine from *Phyllophora nervosa*. *Eczacılık Bülteni* 11: 177-184.
- Güven, K.C., Bora, A. and Sunam, G. (1970). Hordenine from the alga *Phyllophora nervosa*. *Phytochemistry* 9: 1893.
- Hamasaki, N., Shirai, S., Niitsu, M., Kakinuma, K. and Oshima, T. (1993). An alkalophilic bacillus sp. Produces 2-phenylethylamine. *Appl. Environ. Microbiol.* 59: 2720-2722.
- Hanna, C.J and Eyre, P. (1979). On the action of combination bronchodilators. *Agents Actions* 9: 301-309.
- Ivanova, V., Graefe, U., Schlegel, R., Schlegel, B., Gusterove, A., Kol, M., Aleksieva, K. (2003). Isolation and structure elucidation of tyramine and indole alkaloids from Antarctic Starin *Microbispora aerata* IMBAS-11A. *Biotechnol. and Biotechnol. Eq.* 17: 128-132.
- Kneifel, H. (1979). Amine in algae In *Marine algae in Pharmaceutical Science* (H.A.Hoppe, T.Levring, and Y.Tanaka, eds.) Walter, D. E. Gruyter, Berlin, Newyork, pp. 365-401.
- Larghi, E.L. and Kaufman, T.S. (2007). Total synthesis of n-methyl-n-formyltyramine, a new β -phenethylamide derivative iso from *Cyathobasis fruticulosa* (Bunge) Aellen. *Molecular Medicinal Chemistry* 13:26-29.
- Liu, N., Wang, H., Liu, M., Gu, Q., Zheng, W., Huang, Y. (2009). *Streptomyces alni* sp. Nov., a daidzein-producing endophyte isolated from a root of *Alnus nepalensis*. [http://nextbio.com/7b/home.nb?q=N-\(p-Hydroxyphenethyl\)acetamide](http://nextbio.com/7b/home.nb?q=N-(p-Hydroxyphenethyl)acetamide)
- Massicot, J. and Mareon, L. (1957). Biogenesis of alkaloids. XVIII. The formation of hordenine from phenylalanine in barley. *Can. J. Chem.* 35: 1-4.
- McKenna, D.J. (1995). Plant hallucinogens: springboards for psychotherapeutic drug discovery. *Behav. Brain Research* 73: 109-116.
- McCorkindale, N. J. (1977). β -Phenethylamines and the isoquinoline alkaloids. *The alkaloids*. (Saxton, J.E., ed.) Vol. 7. J.W.Arrowsmith Ltd, Bristol. pp. 92-151.
- Paxon, T.L., Powell, P.R., Lee, H.Ç., Eving, K-A.G. (2005). Microcolumn separation of amine metabolites in the fruit fly. *Anal. Chem.* 77: 5349-5355.
- Percot, A., Yalçın, A., Aysel, V., Erduğan, H., Dural, B. and Güven, K.C. (2009). β -phenylethylamine content in marine algae around Turkish coasts. *Botanica Marina* 52: 87-90.
- Percot, A., Yalçın, A., Erduğan, H. and Güven, K.C (2007). Hordenine amount in *Phyllophora nervosa* (D.C.Grev) (Marine Alga) collected from Şile (the Black Sea) and Dardanelle. *Acta Pharm. Sci.* 49: 127-132.
- Rolle, İ., Hobucher, H.E., Kneifel, H., Paschold, B., Riepe, W. and Soeder, C.J. (1977). Amine in unicellular green algae, *Scenedesmus acutus*. *Analytical Biochemistry* 77: 103-109.
- Saavedra, J.M. (1978). β -Phenethylamine: is this biogenic amine related to neuropsychiatric disease? *Mod. Pharmacol. Toxicol.* 12: 139-157.

- Sabelli, H., Fink, P., Fawcett, J. and Tom, C. (1996). Sustained antidepressant effect of PEA replacement. *J. Neuropsychiatry Clin. Neurosci.* 8: 168-171.
- Sakurai, H. (1958). Studies of metabolism in tuberculous lesions. <http://www....search?q=n-acetyltyramine&hl=tr&inlang=tr&ie=UTF-8&start=10&sa=>
- Shabana, M., Gonaïd, M., Salama, M.M. and Abdel- Sattar, E.(2006). Phenylalkylamine alkaloids from *Stapelia hirsuta* L. *Natural Product Research* 20: 710-714.
- Smith, T.A. (1977). Phenethylamine and related compounds in plants. *Phytochemistry* 16: 9-18.
- Snieckus, V.A. (1971). β -Phenethylamines and simple isoquinoline alkaloids. *The Alkaloids*.(Saxton, J.E. ed.) Vol. 1. J.W.Arrowsmith Ltd. Bristol, pp.103-105.
- Sorensson, M.M., Gallo, A.A. and Guillory, C.C. (2004). N-acetyltyramine and 3,5,7- trimethyl-4H-1,2 diazepine are pres in the leaves of American holly, *Ilex opaca*. *J. Undergraduate chemistry Resea.* 3:3. <http://www.vmi.edu/WorkArea/downloadasset.aspx?id=2224>.
- Spencer, I.D. (1970). Biosynthesis of Alkaloids. *Chemistry of Alkaloids* Pelletier, S.W. ed.Van Nostrand Reinhold Cie. pp.669-718.
- Steiner, M. and Hartmann, T. (1968). Über Vorkommen und Verbreitung flüchtiger Amine bei Meeresalgen. *Planta* 79: 113-121.
- Tian-Shung, W.U., Yanna- Lii, L. and Yu-Yi, C. (1999). Constituents of the fresh leaves of *Aristolochia cucurbitifolia*. *Chem. Pharm. Bull.* 47: 571-573.
- Tocher, R.D. and Tocher, C. (1969). Abstr. XI. Int. Bot. Cong. p.219 through ref. Smith, 1977.
- West, L.G., Vanderveen, R.L. and McLaughlin, J.L. (1974). β -Phenethylamines from the genus *Gymnocactus*. *Phytochemistry* 13: 665-666.
- Yalçın, A., Percot, A., Erduğan, H., Çoban, B. and Güven, K.C. (2007). Hordenine from *Gelidium crinale* (Hare ex Turner) Gaillon, Marine algae. *Acta Pharm. Sci.* 49: 213-218.

Received:10.11.2007

Accepted:15.12.2007