

Conium maculatum Intoxication: Literature **Review and Case Report on Hemlock Poisoning**

M.-V. Karakasi^{1,2,3}, S. Tologkos⁴, V. Papadatou⁴, N. Raikos⁵, M. Lambropoulou⁴, P. Pavlidis^{1*}

¹ Lab. of Forensic Sciences ⁴ Lab. of Histology and Embryology School of Medicine Democritus University of Thrace Alexandroupolis, Greece

² Emergency Department General Hospital of Didymoteicho Didymoteicho, Greece

³ Adult Psychiatry Psychiatric Department G. Papanikolaou General Hospital of Thessaloniki Thessaloniki, Greece

⁵ Lab. of Forensic Medicine and Toxicology LIEW.COM Faculty of Medicine Aristotle University Thessaloniki, Greece

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* Corresponding author: Dr. P. Pavlidis, School of Medicine,

Democritus University of Thrace, Dragana 68100 Greece;

^{+ 30 25513 53822 (}voice); pavlidi@med.duth.gr.

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ABSTRACT: The aim of this paper is to highlight the symptomatology in three *Conium maculatum* intoxication incidents, one of which was fatal. A number of studies were reviewed in order to update and summarize the relevant literature on the incidence, sociodemographic variables, method of poisoning, pathophysiology, diagnosis, variables associated with survival and fatality, management, and treatment of *C. maculatum* intoxication as well as the biosynthesis and biological effects of poison hemlock alkaloids. Results show that hemlock poisoning is relatively rare, although incidence varies in different regions, despite its worldwide distribution. Hemlock poisoning is more common in European and especially Mediterranean countries. The majority of the patients are adult males over 38 years of age. The clinical course of hemlock poisoning includes neurotoxicosis, tremor, vomiting, muscle paralysis, respiratory paralysis/failure, rhabdomyolysis, and acute renal failure. The therapeutic management focuses on absorption reduction, close observation for complications, and supportive therapy (especially for respiration). Acute occurrence is severe and life-threatening, but the survival rate is high if treatment is provided prompty. Recovery is rapid, generally taking only a few days.

KEYWORDS: Acute, alkaloids, γ-coniceine, coniine, *Conium maculatum*, cowbane, forensic pathology, forensic science, hemlock, intoxication, neuromuscular blockage, neurotoxin, poisoning.

INTRODUCTION

History of the Plant

Conium maculatum (poison hemlock) (**Figure 1**) is known as one of the most poisonous herbaceous plants and has historically been linked to various deaths. It is considered to have been used during classical antiquity for killing older or handicapped men that were unable to work. Hemlock is a poison strongly associated with ancient Greece, mainly due to its use to execute the great philosopher Socrates (399 IICL). However, there had been reported cases of hemlock poisoning that preceded that of Socrates [46].

The first reported death by hemlock in ancient Greece was that of Thiramenes (404 BCE) during the Athenian rule of the Thirty Tyrants. The general and politician Thiramenes was condemned to death and forced to drink hemlock by Critias, a rival member of the Thirty Tyrants driven by ambition for power and characterized by violence. According to the legend, Thiramenes, after having drunk the poison, spilled the last drops on the ground, while prophetically asserting that the latter would be destined

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Figure 1. Sketch of the plant *Conium maculatum* portraying leaves, flowers, seeds, stem, and roots — Based on artworks of William Curtis (1746–1799 and Carl Axel Magnus Lindnus (1856–1928).

for his rival, Critias. Not long after Thiramenes's forced suicide, Critias's killing followed, liberating ancient Athens from oligarchy. Thiramenes was the first case in history of hemlock being used to execute a prisoner, paving the way for Socrates's way of dying [46]. Other historically known cases of execution by hemlock were the deaths of rhetorician Aeschines in 323 BCE, politician Phocion in 318 BCE, and Iustinus Martyr in 167 CE [46].

Poison hemlock was called "κώνειον" (kóneion) by the Greeks, meaning to "whirl about", because of its consumption causing vertigo, ataxia, tremor, and convulsions. The Romans at first used the name *Cicuta* for many different poisonous plants of the same family. That name, however,

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- 53. Penny RH: Hemlock poisoning in cattle; *Vet Rec* 65:669; 1953.
- 54. Poswillo D: Observations of fetal posture and causal mechanisms of congenital deformity of palate, mandible and limbs; *J Dental Res* 45:584; 1966.
- 55. Radulović N, Dorđević N, Denić M, Pinheiro MM, Fernandes PD, Boylan F: Anovel toxic alkaloid from poison hemlock (*Conium maculatum* L., Apiaceae): Identification, synthesis and antinociceptive activity; *Food Chem Toxicol* 50:274; 2012.
- 56. Reynolds T: Hemlock alkaloids from Socrates to poison aloes; *Phytochemistry* 66:1399; 2005.
- 57. Rizzi D, Basile C, Di Maggio A, Sebastio A, Introna F Jr, Rizzi R, Scatizzi A, De Marco S, Smialek JE: Clinical spectrum of accidental hemlock poisoning: neurotoxic manifestations, rhabdomyolysis and acute tubular necrosis; *Nephrol Dial Transplant* 6:939; 1991.
- 58. Roberts MF, Brown RT: A new alkaloid from South African Conium species; *Phytochemistry* 20:447; 1981.
- 59. Seawright AR: *Animal Health in Australia: Chemical and Plant Poisons*, Vol 2; Australian Government Publishing Service: Canberra, Australia; p 28; 1982.
- 60. Smith ML, Vorce SP, Holler JM, Shimomura E, Magluilo

J, Jacobs AJ, Huestis MA: Modern instrumental methods in forensic toxicology; *J Anal Toxicol* 31:237; 2007.

- 61. Tsironi M, Andriopoulos P, Xamodraka E, Deftereos S, Vassilopoulos A, Asimakopoulos G, Aessopos A: The patient with rhabdomyolysis: Have you considered quail poisoning? *Can Med Assoc J* 171:325; 2004.
- 62. Vetter J: Poison hemlock (*Conium maculatum* L.); *Food Chem Toxicol* 42:1373; 2004.
- 63. Wertheim T: Über ein neues Alkaloïd in Conium maculatum; *Liebigs Ann* 100:328; 1856.
- 64. West PL, Horowitz BZ, Montanaro MT, Lindsay JN: Poison hemlock-induced respiratory failure in a toddler; *Pediatr Emerg Care* 25:761; 2009.
- 65. Widmer WR: Poison hemlock toxicosis in swine; *Vet Med* 79:405; 1984.
- 66. Wolffenstein R: Über Conium-Alkaloïde; Berichte der Deutschen Chemischen Gesellschaft 27:2611; 1894.
- 67. Wolffenstein R: Über Conium-Alkaloïde; Berichte der Deutschen Chemischen Gesellschaft 28:302, 1895.
- World Health Organization: World Report on Child Injury Prevention. Children and Poisoning; http://www.who.int/ violence_injury_prevention/child/en/ (Accessed January 24, 2018).

ABOUT THE AUTHORS M.-V. Karakasi; S Tologkos; V. Papadatou; N. Raikos; M. Lamb o poulou; P. Pavlidis

Maria-Valeria Karakasi holds a medical degree (M.D.) and a license to practice from Democritus University of Thrace (Thrace, Greece). Dr. Karakasi is currently a doctoral student in the Laboratory of Forensic Sciences at the same university. She has completed three years of residency in adult psychiatry in Papanikolaou General Hospital of Thessaloniki (Thessaloniki, Greece) and is currently practicing emergency medicine in the General Hospital of Didymoteicho (D dymoteicho, Greece). Her research interests focus on forensic psychiatry, issues of autonomy, suicidal behavior, sexual homicide, homicide, antisocial behavior, puerperal mental disorders, and drug abuse disorder.

tylianos Tologkos holds a degree in molecular biology and genetics from Democritus University of Thrace. He is currently a master's degree student in the faculty of Molecular Biology and Genetics at the same university, and also works voluntarily in the Laboratory of Histology and Embryology there. His research interests focus on histological and immunohistochemical evaluation of tissue samples, modern molecular technologies in the diagnosis and treatment of infectious diseases, molecular developmental biology, molecular immunology and neurobiology, regulation of gene expression, biochemistry, human genetics, bioinformatics, and physiology.

Vasiliki Papadatou holds a degree in molecular biology and genetics from Democritus University of Thrace. She is currently a master's degree student in the faculty of Molecular Biology and Genetics at the same university, and also works voluntarily in the Laboratory of Histology and Embryology there. Her research interests focus on histological and immunohistochemical evaluation of tissue samples, modern molecular technologies in the diagnosis and treatment of infectious diseases, molecular developmental biology, molecular immunology and neurobiology, regulation of gene expression, biochemistry, human genetics, bioinformatics, and physiology.

Nikolaos Raikos holds a degree in chemistry (Department of Chemistry) and a medical degree (M.D.) as well as a license to practice (Faculty of Medicine) from Aristotle University of Thessaloniki (Thessaloniki, Greece). Dr. Raikos also has a Ph.D. from the Aristotle University Faculty of Medicine and is currently an associate professor of

forensic medicine and toxicology there, as well as head of its Laboratory of Forensic Medicine and Toxicology. Dr. Raikos is a licensed forensic toxicologist and a court-appointed expert in matters relating to the legal investigation of death, poisoning, and drug use. His research expertise focuses on mass spectrometry, high-performance figure chromatography, solid phase extraction, tandem mass spectrometry, and drug analysis.

Maria Lambropoulou holds a medical degree (M.D.), a license to practice, and a Ph.D. from Democritus University of Thrace. Dr. Lambropoulou is currently an associate professor of histology and emoryology and head of the Histology and Embryology Department at the Democritus University School of Medicine. Dr. Lambropoulou has conducted extensive scientific research, with research interests on application of molecular techniques for the study of tissues that contribute to the differential diagnosis of various diseases, histochemistry, immunohistochemistry, cytochemistry, immunofluorescence, PCR, ISH, electron meroscopy, molecular histopathology of malignant neoplasms and various diseases, experimental histopathology, endometrial death investigation, molecular approach of congenital embryonic abnormalities, and placental pathology.

Pavlos Pavlidis holds a medical degree (M.D.) from the Faculty of Medicine, Trakia University (Stara Zagora, Bulgaria) and a Ph.D. from the Faculty of Medicine, Aristotle University of Thessaloniki (Thessaloniki, Greece). He also has a master's degree in occupational health from Democritus University of Thrace. Dr. Pavlidis is currently an assistant professor of forensic medicine and toxicology and head of the Laboratory of Forensic Sciences at School of Medicine, Democritus University of Thrace. Dr. Pavlidis is a licensed forensic pathologist and a court-appointed expert in matters relating to homicide, suicide, occupational accidents, rape, child abuse, domestic violeuce, (migration) border-related deaths, and toxicology. He is a frequent consultant to the national media and international press involving numerous newspaper articles and international documentaries. His published work includes a monograph: Pavlidis P: *Elements of Medical Law, Ethics and Problematic*; Publications Utopia: Athens, Greece; 2008.

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