ejbps, 2020, Volume 7, Issue 7, 701-710. *Review Article* SJIF Impact Factor 6.044

EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 7
701-710
Year: 2020

MYSTERY OF OBNOXIOUS SMELLING DIAMINO ALKANE VOLATILE GASES: CADAVER, CADAVERINE AND PUTRESCINE

Subham Chakraborty*, Joyeta Ghosh, Dhrubajyoti Bardhan, Arpita Biswas, Dr. Dhrubo Jyoti Sen, Dr. Beduin Mahanti

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

***Corresponding Author: Subham Chakraborty**
Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

Article Received on 20/05/2020 **Article Revised on 11/06/2020** **Article Accepted on 02/07/2020**

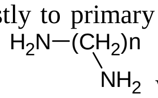
ABSTRACT

Diamino alkanes in volatile species: Cadaver, Cadaverine and Putrescine gases: Do you know what are diamino alkanes volatile gases? Basically, these are obnoxious smelling volatile gases, Cadavers are liberated from deadly human bodies or decomposed matters. Cadavers are volatile gases and are used by Medical Students for studying the anatomy, to identify disease sites and to determine the cause of deaths. These gases are obtained from unclaimed bodies i.e., those who died without any witnesses and discovered by two ancient Greece scientists Herophilon of Chalcedon and Erasistratus of Ceos. Maximum students use Cadavers for suturing each body part of dead bodies and lastly, they are returned to their family for cremation. Infectious Pathogens in Cadavers include tuberculosis, Hepatitis B, HIV etc., and the chemicals like formaldehyde, phenol, methanol and glycerine are used to preserve Cadavers. Cadaverine are alpha alkane, omega diamine straight chain core with amino substituents at 1st and 5th positions. It was discovered by Berlin Physicians in 1885. For microbial fermentation, Cadaverine strains are engineered by L-Lysine. Lysine is decarboxylated to Cadaverine in the presence of enzyme Lysine decarboxylase. It has tremendous effects on plants and animals and shows its large toxicity range. Cadaverine found in some plants in trace amount to attract strangers and acts as a tool for training search and dogs. Different diseases for cadaverine gases are Kidney disease, Leukaemia etc. and EMT gene is regulated upon its treatment. Whereas, Putrescine is a four-carbon alkane omega diamine, obtained by amino acid breakdown and have foul odour of putrefying fish. This gas has high toxicity range when decomposed, it releases fumes of NOx. It plays multifunctional role in cell-growth, differentiation, and cell growth. Polyamines also play role in cellular processes, migration and mucosal maturation. Putrescine also influences RNA stabilization and transitional frame-shifting.

KEYWORDS: Cadaver-graft, bio-based polyamides, microbial fermentation, amino acid breakdown, self-digestion, bloating, putrefaction, unclaimed bodies, warranted, Plastination, polymerization reaction, Metabolism, Anaerobiosis, biosynthesis, Methionine, Duraboline, Toxicity, Catabolism, EMT (Endothelial to Mesenchymal transition) genes, putrefying flesh, DSM, Biochemistry, ODC (Ornithine Decarboxylase), flexible polycationic nature, cellular processes, RNA stabilization, Transitional frame-shifting.

Diamino alkanes in volatile species: Cadaver gas

Introduction: A diamine is an amine with exactly two amino groups. Diamines are used as monomers to prepare polyamides, polyimides, and polyureas. The term diamine refers mostly to primary diamines, as those are the most reactive.



When n=0: hydrazine, n=1: methanediamine, n=2: ethylenediamine, n=3: diaminopropane, n=4: putrescine, n=5: cadaverine. N=6: hexamethylenediamine.

Aliphatic diamines: [Linear: 1 carbon: methanediamine (diaminomethane), 2 carbons: ethylenediamine (1,2-diaminoethane), 3 carbons: 1,3-diaminopropane (propane-1,3-diamine), **4 carbons: putrescine (butane-1,4-diamine), 5 carbons: cadaverine (pentane-1,5-diamine)**, 6 carbons: hexamethylenediamine (hexane-1,6-diamine), trimethylhexamethylenediamine. Branched: Derivatives of ethylenediamine are prominent: 1,2-diaminopropane, which is chiral, diphenylethylenediamine, which is C2-symmetric, trans-1,2-diaminocyclohexane, which is C2-symmetric]

Cyclic [1,4-Diazacycloheptane, 1,4-Diazacycloheptane]

Xylylenediamines [o-xylylenediamine or OXD, m-xylylenediamine or MXD, p-xylylenediamine or PXD]

Aromatic diamines [o-phenylenediamine or OPD, m-phenylenediamine or MPD, p-phenylenediamine or PPD]

A cadaver is a dead human body that is used by medical students, physicians and other scientists to study anatomy, identify disease sites, determine causes of death, and provide tissue to repair a defect in a living human being. Students in medical school study and dissect cadavers as a part of their education. Others who study cadavers include archaeologists and artists. The Cadavers are mostly used in Courts of Law, where it is referred to a dead body as well as by recovery items searching for bodies in Natural Disaster.

Justification: Do you know why it is so called?
The word comes from the Latin word **Cadere** which means **to fall**. A cadaver graft (also called "post-mortem graft") is the grafting of tissue from a dead body onto a living human to repair a defect or disfigurement. Cadavers can be observed for their stages of decomposition, helping to determine how long a body has been dead. Cadavers have been used in art to depict the human body in paintings and drawings more accurately. They are obnoxious invisible volatile compounds.[1]

Stages of Decomposition
• The first stage is **Autolysis**: More commonly known as self-digestion, during which the body's cells are destroyed through the action of their own digestive enzymes. However, these enzymes are released into the cells because of active processes ceasing in the cells, not as an active process. In other words, though autolysis resembles the active process of digestion of nutrients by live cells, the dead cells are not actively digesting themselves as is often claimed in popular literature and as the synonym of autolysis-self-digestion-seems to imply. As a result of autolysis liquid is created that seeps between the layers of skin and results in peeling of the skin. During this stage, flies (when present) begin to lay eggs in the openings of the body: eyes, nostrils, mouth, ears, open wounds, and other orifices.[2]

Figure-1: Autolysis, Bloating & Putrefaction: Stages of body decomposition.

- The second stage of Decomposition is **Bloating**: Bacteria in the gut begins to break down the tissues of the body, releasing gas that accumulates in the intestines, which becomes trapped because of the early collapse of the small intestine. This bloating occurs largely in the abdomen, and sometimes in the mouth, tongue, and genitals. This usually happens around the second week of decomposition. Gas accumulation and bloating will continue until the body is decomposed sufficiently for the gas to escape.
- The third stage is **Putrefaction**: It is the final and longest stage. Putrefaction is where the larger structures of the body break down, and tissues liquefy. The digestive organs, brain, and lungs are the first to disintegrate. Under normal conditions, the organs are unidentifiable after three weeks. The muscles may be eaten by bacteria or devoured by animals. Eventually, sometimes after several years, all that remains is the skeleton. In acid-rich soils, the skeleton will eventually dissolve into its base chemicals.

This is in brief about the stages of decomposition of Cadaver volatile compounds.

Factors
The rate of Decomposition depends of Cadaver volatile compounds depends on the following points:
- Temperature
- Environment

The warmer and more humid the environment, the faster the body is broken down. The presence of carrion-consuming animals will also result in exposure of the skeleton as they consume parts of the decomposing body.

How long does a Cadaver Last?
A Cadaver settles over the three months after embalming, dehydrating to a normal size. By the time it's finished, it could last up to six years without decay. The face and hands are wrapped in black plastic to prevent them from drying, an eerie sight for medical students on their first day in the lab.

Sources of Cadaver: Most common sources are body donation programs and "unclaimed" bodies—that is, bodies of individuals who die without relatives or friends to claim them for burial or without the means to afford burial. In some countries with a shortage of available bodies, anatomists import Cadavers, from other countries.[3]

History of Cadaver: The history of the use of cadavers is one that is filled with controversy, scientific advancements, and new discoveries. It all started in 3rd century ancient Greece with two physicians by the name of Herophilus of Chalcedon and Erasistratus of Ceos. They practiced the dissection of cadavers in Alexandria, and it was the dominant means of learning anatomy. After both of these men died the popularity of anatomical dissection decreased until it wasn't used at all. It wasn't revived until the 12th century and it became increasingly popular in the 17th century and has been used ever since. In light of the new discoveries and advancements that were being made religious moderation of dissection relaxed significantly, however the public perception of it was still negative. Because of this perception, the only legal source of cadavers was the corpses of criminals who were executed, usually by hanging. Many of the offenders whose crimes "warranted" dissection and their families even considered dissection to be more terrifying and demeaning than the crime or death penalty itself. There were many fights and sometimes even riots when relatives and friends of the deceased and soon to be dissected tried to stop the delivery of corpses from the place of hanging to the anatomists. The government at the time (17th century) took advantage of these qualms by using dissection as a threat against committing serious crimes. They even increased the number of crimes that were punished by hanging to over 200 offenses. Nevertheless, as dissection of cadavers became even more popular, anatomists were forced to find other ways to obtain cadavers. It was found that the cost of dying was incredibly high and a large amount of funeral homes were scamming people into paying more than they had to. These exposures didn't necessarily remove stigma but created fear that a person and their families would be victimized by scheming funeral directors, therefore making people reconsider body donation. Currently, body donation isn't surrounded by stigma but can be considered as celebrated. Body donation has not only led to scientific advancements and discoveries, it has also led to lives being saved.[4]

Effects of Cadavers on Human Body: This Obnoxious Smelling volatile gas has following irritable impacts on Human Health. Most of medical students complained of symptoms of acute exposure to formalin-treated cadavers such as:

- Unpleasant smell (91.2%),
- Dry or sore nose (74.2%),
- Running or congested nose (69.5%),
- Unusual thirst (53.9%),
- Itching in the eyes (81.3%),
- Redness in the eyes (72.4%),
- Excessive lacrimation (76.1%) etc.

Importance of Cadaver in dissection: For a cadaver to be viable and ideal for anatomical study and dissection, the body must be refrigerated or the preservation process must begin within 24 hours of death. This preservation may be accomplished by embalming using a mixture of embalming fluids, or with a relatively new method called Plastination. Both methods have advantages and disadvantages in regards to preparing bodies for anatomical dissection in the educational setting.

Effect of Cadaver gas in Medical field: In present-day times, cadavers have become more and more popular within the medical and surgical community to gain further knowledge on human gross anatomy. Surgeons have dissected and examined cadavers before surgical procedures on living patients to identify any possible deviations within the surgical area of interest. New types of surgical procedures can lead to numerous obstacles involved within the procedure which can be eliminated through prior knowledge from the dissection of a cadaver. Cadavers not only provide medical students and doctor's knowledge about the different functions of the human body, but they also provide multiple causes of malfunction within the human body. Galen (250 AD), a Greek physician, was one of the first to associate events that occurred during a human's life with the internal ramifications found later after death. A simple autopsy of a cadaver can help determine origins of deadly diseases or disorders. Autopsies also can provide information on how certain drugs or procedures have been effective within the cadaver and how humans respond to certain injuries. Appendectomies, the removal of the appendix, are performed 28,000 times a year in the United States and are still practiced on human cadavers and not with technology simulations. Gross anatomy, a common course in medical school studying the visual structures of the body, gives students the opportunity to have a hands-on learning environment. The need for cadavers has also grown outside of academic programs for research. Organizations like Science Care and the Anatomy Gifts Registry help send bodies where they are needed most.[5]

Do you know the smelling of Cadaver? Cadaver gases and compounds produced in a decomposing body emit distinct odours. While not all compounds produce odours, several compounds do have recognizable odours, including: **Cadaverine** and **Putrescine** smell like rotting flesh.

Uses of Cadaver: Every student has to use Cadaver painstakingly suture each body part back together. Professors would only accept the best and sincere efforts. The cadavers are then returned to their families to be cremated. However, the university took one step further!

Probability of getting affected by diseases from Cadaver: Infectious pathogens in cadavers that present particular risks include *Mycobacterium tuberculosis*, hepatitis B and C, the AIDS virus HIV, and prions that cause transmissible spongiform encephalopathies such as Creutzfeldt-Jakob disease (CJD) and Gerstmann-Straussler-Scheinker syndrome (GSS).

Preservation of Cadaver Gas: A number of chemicals are used in various proportions to preserve cadavers. The main chemicals are typically: formaldehyde, phenol, methanol, and glycerine.... It is part of the embalming solution at a 3.0% concentration.

Do you know the sterility of Cadaver Gases? For medical students, nothing can replace practicing on cadavers that are as lifelike as possible.... It produces sterile, fungus-free cadavers that look and feel as close as possible to a living body.

Public Views of Cadaver crash test dummies: After a New York Times article published in 1993, the public became aware of the use of cadavers in crash testing. The article focused on a Heidelberg University's use of approximately 200 adult and children cadavers. After public outcry, the university was ordered to prove that the families of the cadavers approved their use in testing.[6]

Plastination: Whole-body plastination begins with much the same method as traditional embalming; a mixture of embalming fluids and water are pumped through the cadaver via arterial injection. After this step is complete, the anatomist may choose to dissect parts of the body to expose particular anatomical structures for study. After any desired dissection is completed, the cadaver is submerged in acetone. The acetone draws the moisture and soluble fats from the body and flows in to replace them. The cadaver is then placed in a bath of the plastic or resin of the practitioner's choice and the step known as forced impregnation begins. The bath generates a vacuum that causes acetone to vaporize, drawing the plastic or resin into the cells as it leaves. Once this is done the cadaver is positioned, the plastic inside it is cured, and the specimen is ready for use. The method of Cadaver preservation involves the replacement of fluids and soluble lipids in body with plastics. These are called Plastinates.

Advantages and Disadvantages of Cadaver on using Plastination: Plastinates are advantageous in the study of anatomy as they provide durable, non-toxic specimens that are easy to store. However, they still have not truly gained ground against the traditionally embalmed cadaver. Plastinated cadavers are not accessible for some institutions, some educators believe the experience gained during embalmed cadaver dissection is more valuable, and some simply do not have the resources to acquire or use plastinate. While many cadavers were murderers provided by the state, few of these corpses were available for everyone to dissect.

Cadaveric effects on Sense Organs: Various preservation methods have been devised to prolong the storage of human cadavers that are donated for research and training purposes. However, the majority of these embalming solutions fail to maintain the structure of the human cadaveric bulbi oculi intact, as they have a tendency to become deflated and dehydrated post-mortem. In fact, as a result, many ophthalmic surgery tuition centres are currently resorting to the use of fresh animal eyes to aid their students in mastering ocular surgical techniques. The objective of this literature review is to identify methods that warrant further investigation as they may aid in devising effective preservation techniques for the human cadaveric eye. Methods that can possibly be applied to increase the intra-ocular pressure and prevent deflation of the human cadaveric eye include: the administration of increased fluid injections to increase volume, application of the head-down tilt, cauthery or clamping of the optic nerve and ophthalmic vessels, induction of corneal rigidity as well as alteration of angle closure and cerebrospinal fluid pressure. Moreover, several corneal artificial hydration solutions exist that warrant further experimentation to establish if they can also be used to prevent dehydration of the human cadaveric eye. These include: hyaluronic acid or carboxymethylcellulose-based solutions, trehalose-based solutions, hydroxypropyl-guar or Hypromellose-based solutions as well as hypotonic or isotonic saline.[7]

The skin accumulation of therapeutic agents affects the efficiency of topical drug delivery. In this study, *in-vitro* distribution of finasteride of ethosomes and liposomes in human cadaver skin after percutaneous delivery were investigated. The finasteride accumulation in ethosomes group showed a distinctive reversed distribution profile. This distinctive reversed distribution profile is meaningful for exerting a favourable pharmacological effect for finasteride. The drug distribution profile in skin layers showed no significant difference between 12- and 24-hours application ($p > 0.05$). The study demonstrated that finasteride can be accumulated at target site more effectively and maintained at higher level through the application of novel ethosomal carriers.

Diamino Alkanes in Volatile Species

Cadaverine: 

Introduction: Cadaverine is an alkane-alpha, omega-diamine comprising a straight-chain pentane core with amino substituents at positions 1 and 5. Cadaverine was first described in 1885 by the Berlin physician Ludwig Brieger (1849–1919). Cadaverine is a toxic diamine with the formula $NH_2(CH_2)_5NH_2$ having the molecular weight of 102.18 g/mol. Cadaverine is also known by the names 1,5-pentanediamine and pentamethylenediamine. Pentolinium and pentamethonium are both chemical derivatives of cadaverine. It is a lysine catabolite involved in plant growth and development. Cadaverine has a similar structure to the synthesized petrochemical hexamethylenediamine, and thus can be used to replace hexamethylenediamine in the production of polyamides or polyurethanes. Cadaverine is becoming an important industrial chemical because it exhibits broad prospects for various applications, and especially for the synthesis of fully bio-based polyamides by polymerization with dicarboxylic acids derived from renewable sources. At present, cadaverine can be produced by direct microbial fermentation or whole-cell bioconversion. For direct microbial fermentation, cadaverine-producing strains are mainly engineered from the conventional L-lysine producers *Corynebacterium glutamicum* and *Escherichia coli*, because L-lysine is the direct precursor of cadaverine. It is formed through the direct decarboxylation of L-lysine catalysed by lysine decarboxylase, and that is widely distributed in prokaryotes and eukaryotes. Cadaverine plays an important role in cell survival at acidic pH and protects cells that are starved of inorganic phosphate, Pi, under anaerobic conditions. In plants, it is involved in regulating diverse processes such as plant growth and development, cell signalling, stress response, and insect defence. Cadaverine formation is also related to animal growth and tumorigenesis.[8]

Structure

Cadaverine is a structural derivative ammonia.

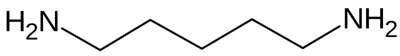


Figure-2: 2D Structure.

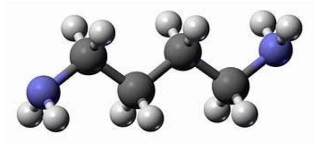


Figure-3: 3D Structure.

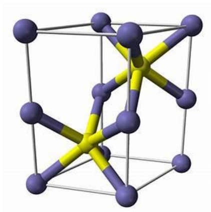


Figure-4: Crystal Structure.

Chemistry: Chemical formula: $C_5H_{14}N_2$, Molar mass: 102.81 g/mol, Density: 0.8730 g/mL, Melting point: 11.83℃ (53.29°F; 284.98K), Boiling point: 179.1°C (354.3°F; 452.2K), Solubility: Soluble in water, Appearance: Colourless to yellow oily liquid, Odour: Unbearably unpleasant to unpleasant, Acidity (pKa): 10.25, 9.13, Refractive index: 1.458.

Methods of Preparation: Cadaverine is a carrion odour produced by microbial metabolism of the amino acid lysine. Cadaverine is a foul-smelling diamine compound produced by the putrefaction of animal tissue. It is also produced by the process of decarboxylation of the amino acid, lysine (where, the raw material lysine is preferably a free base i.e. lysine base). Here, L-lysine is usually preferred. Cadaverine dicarboxylate is produced by performing an enzymatic (Lysine decarboxylase) decarboxylation reaction of a lysine solution while adding a dicarboxylic acid, containing 4 to 10 carbons to the lysine solution to maintain pH of the solution at a level sufficient for the enzymatic decarboxylation reaction to occur. For example, 4.0-8.0. According to the present invention, cadaverine dicarboxylate can be simply and efficiently produced in the way where the cadaverine dicarboxylate obtained by the present invention can be used in a polymerization reaction for producing nylon.[9]

Lysine Cadaverine

Figure-5: Reaction for the production of Cadaverine from Lysine.

Metabolism of Cadaverine: Lysine serves as a precursor for cadaverine, and is critical for fatty acid metabolism, the citric acid cycle, and amino acid synthesis. Cadaverine can be conjugated to phenolics, or used to construct higher-order polyamines. Cadaverine can also be oxidized, or converted to quinolizidine alkaloids. Bound cadaverine may affect cell-wall properties, membrane stability, gene expression and nucleic acid stability. The metabolism of Cadaverine have been extensively studied in *E. coli*. Cadaverine metabolism was investigated in vitro in several organs of the mouse by measuring $14CO_2$ formation from labelled precursors. The liver showed the highest formation of 14CO from [1,5-14C]-Cadaverine, whereas brain demonstrated a much lower formation. Anaerobiosis or inhibition of monoamineoxidase (MAO) activity significantly reduced $14CO_2$ formation in every organ, but inhibition of diamine oxidase (DAO) activity had no effect in brain and kidney.

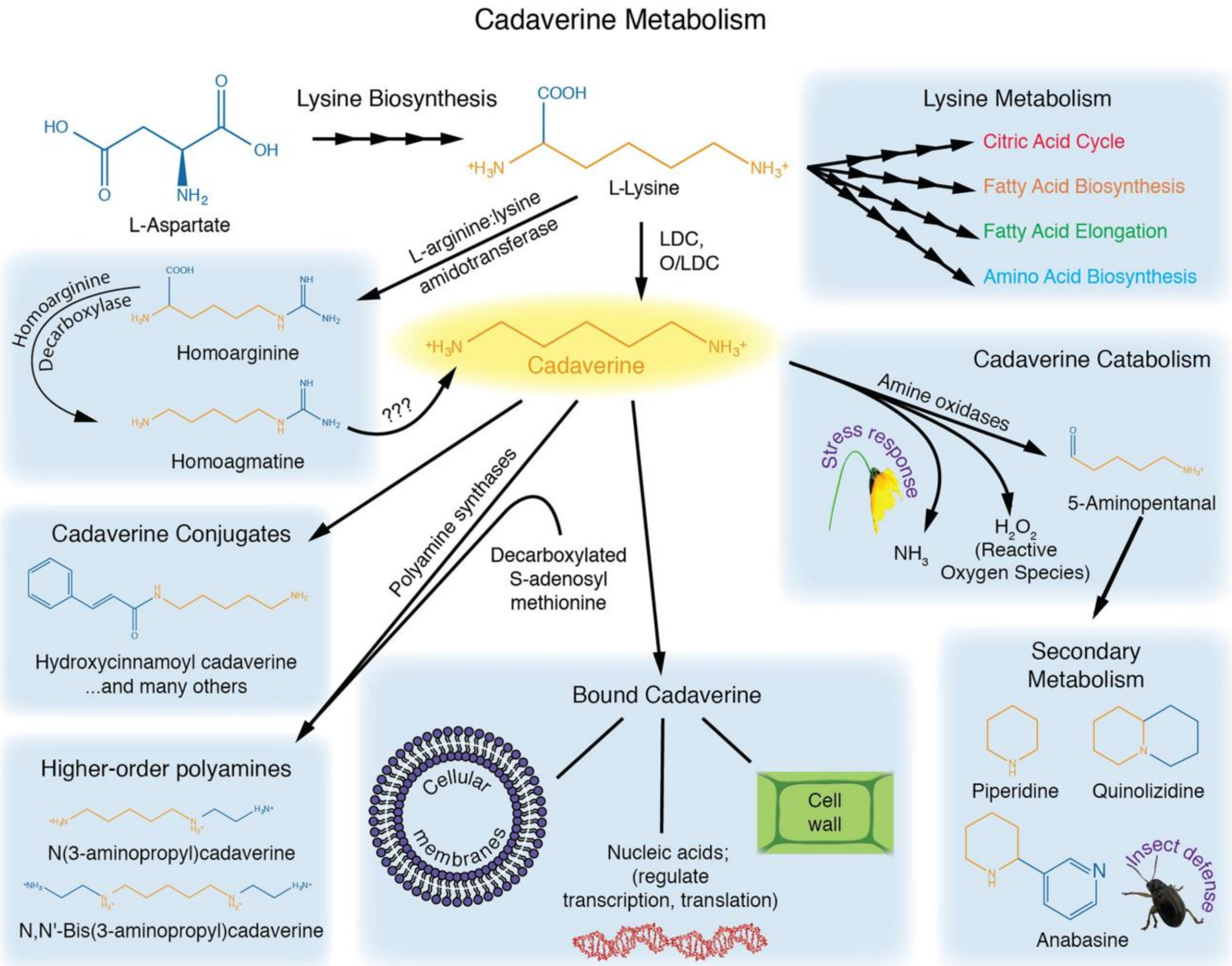


Figure-6: Cadaverine metabolism.

Piperidine was formed from Cadaverine *in-vitro* only in the large intestine and its content. This formation is probably of bacterial origin. Under a variety of experimental conditions, we were unable to demonstrate any formation of piperidine in brain from Cadaverine. Outside the brain, formation of piperidine from pipecolic acid is detectable only in kidney and in the content of the large intestine. The latter is probably of bacterial origin.[10]

CATABOLISM OF CADAVERINE

Biosynthesis

Cadaverine has independent single exclusive biosynthetic pathway in all organisms. The synthesis of Cadaverine from lysine is also proposed as by product of methionine synthesis through aspartate pathway. However, the lysine decarboxylation by LDC (Lysine decarboxylase) is taking place through pyridoxyal phosphate but there are few exceptions. Like under ornithine deficiency, ODC (Ornithine decarboxylase) can use lysine as an alternate substrate for Cadaverine synthesis. Biosynthesis of Cadaverine in Mice under the Influence of an Anabolic Steroid:

Cadaverine (1, 5-diaminopentane) in the kidney and urine was investigated in mice treated with the anabolic steroid Durabolin (nandrolone phenpropionate). After administration of this steroid cadaverine was found in the kidneys, whereas this amine could not be detected in the kidney of controls and the urinary excretion of Cadaverine was elevated 50 times after the administration of Durabolin into the body of mice.

Catabolism: Catabolism of polyamines takes place through amine of oxidases, acting as enzymes. Oxidation of Cadaverine is primarily through diamine oxidase in apoplast, leading to the production of 5-aminobutanal, ammonia and H_2O_2. The diamines oxidase has a low rate of catabolising Cadaverine. The regulation of DAO (diamine oxidase) in different plants could be different.

The Arabidopsis genome mapping revealed total 12 diamine oxidases genes out of which ATAO1 is characterized. Apparently there appears to be linked between inhibitors of Cadaverine synthesis and diamine oxidases and DFMO (Difluoromethylornithine). Non-specific effect on Cad synthesis indicates indirect regulation of polyamines contents depending on plant species and physical condition.[11]

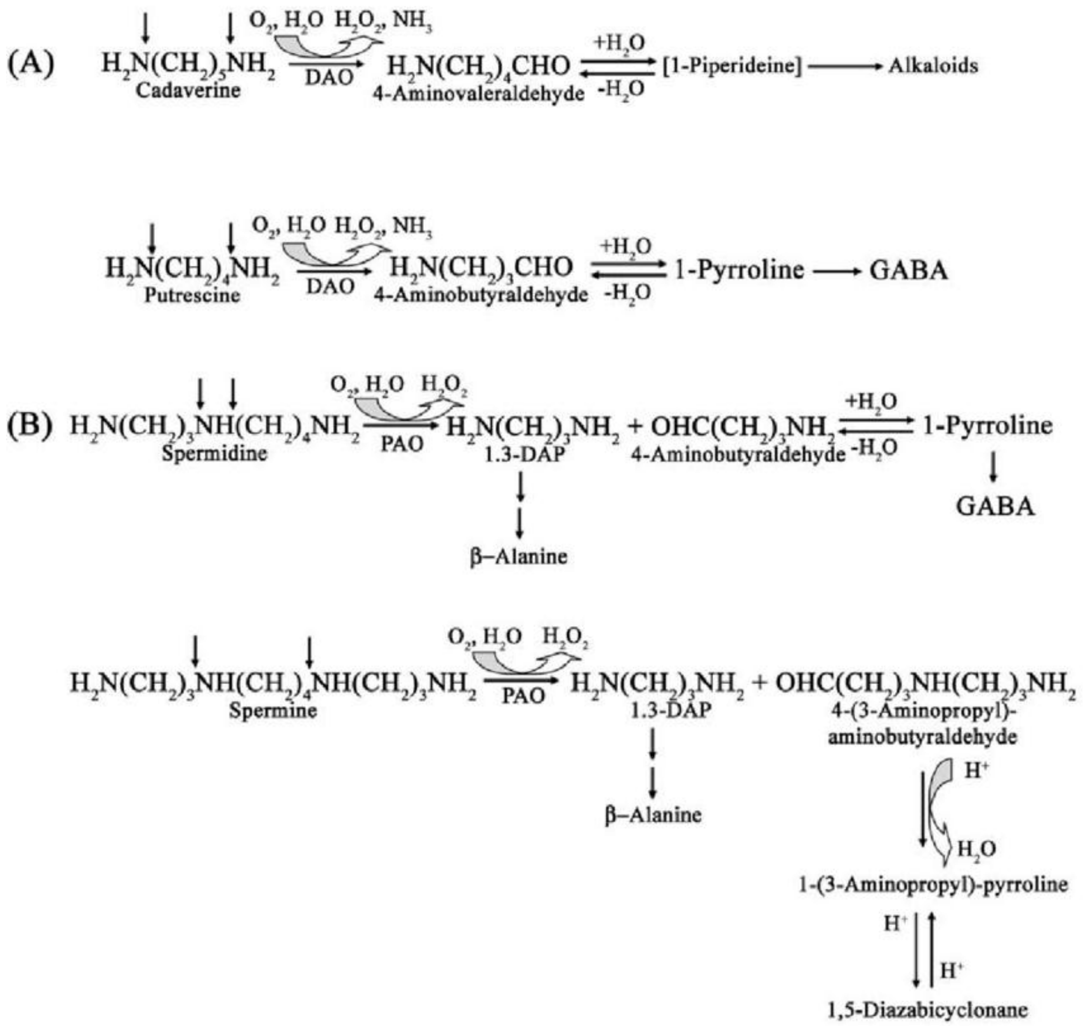


Figure-7: Cadaverine Biosynthesis and Catabolism.

Role of Cadaverine

On Plants: Cadaverine (Cad) a diamine, amino compound produced as a lysine catabolite is also implicated in growth and development of plants depending on environmental condition. For example, the Leguminosae have been shown to produce cadaverine and use it as a precursor in the biosynthesis of quinolizidine alkaloids, secondary metabolites that are involved in insect defence and also display therapeutic pharmacological properties. Cadaverine is also present in the environment; it can be produced by rhizosphere and phyllosphere microbes. Markedly, exogenous cadaverine application causes alterations in root-system architecture.

On Animals: In *Escherichia coli*, Cadaverine is used to mediate acid stress (Haneburger et al., 2012), and the deathly odour of Cadaverine provides behavioural cues to animals (Rolen et al., 2003; Hussain et al., 2013). Cadaverine functions in a multitude of cellular processes critical to living organisms. Elevated levels of cadaverine have been found in the urine of some patients with defects in lysine metabolism. The odour commonly associated with bacterial vaginosis has been linked to cadaverine and putrescine.[12]

Toxicity: Cadaverine shows its toxicity in large doses. In rats, it has a low acute oral toxicity of 2,000 mg/kg body weight; its no-observed-adverse-effect level is 2,000 ppm (180 mg/kg body weight/day). Cadaverine are largely responsible for the foul odour of putrefying flesh, but also contribute to the odour of such processes as bad breath, etc.

Uses

- Cadaverine, found in some plants in trace amount as a result of stress on the plant is sold in some hunting

supply stores as a poisonous liquid as it has the capability to attract strangers.
- It is also used as a tool for training search and dogs.

Clinical Significance: Elevated levels of Cadaverine have been found in the urine of some patients with defects in lysine metabolism. The odour commonly associated with bacterial vaginosis has been linked to Cadaverine. Its presence is responsible for the odours of urine and semen.[13]

Diseases: Diseases associated with the presence of Cadaverine at different levels are: Kidney disease, Irritable bowel syndrome, Ulcerative colitis, Colorectal cancer, Crohn's disease, Perillyl alcohol administration for cancer treatment, Pancreatic cancer, Periodontal disease, Thyroid cancer, Leukemia.

Treatment: List of EMT (Endothelial-to-mesenchymal transition) genes differentially regulated upon Cadaverine treatment.

Abbreviation	Gene name	Category
MMP2	Matrix Metalloproteinase 2	Extracellular matrix and cell adhesion
MMP3	Matrix Metalloproteinase 3	
MMP9	Matrix Metalloproteinase 9	
Krt14	Keratin 14	
CDH1	E-cadherin	
Spp1	Secreted Phosphoprotein 1	
FgfBp1	Fibroblast Growth Factor Binding Protein 1	Cell growth and proliferation
Notch1	Notch 1	
Tgfb3	Transforming Growth Factor Beta 3	
Erbb3	Human Epidermal Growth Factor Receptor 3	
Esr1	Oestrogen Receptor 1	
IgfBp4	Insulin Like Growth Factor Binding Protein 4	

Putrescine

Introduction: A field experiment was conducted in the north western part of Kom Osheem district, Tamiya Town, El- Fayoum Governorate, Egypt to study the possibility of using potassium foliar spray of (K_2SO_4) at rate of 1000L/ ha-1 twice after one month from sowing and at one month later and putrescine (1,4-Diaminobutane dihydrochloride) foliar spray of 10 u M solution, The putrescine was sprayed in two equal doses, one dose after one month from the sorghum sowing and the second dose one month later at rate of 1000L/ ha-1., to mitigate the negative effect of irrigation with mixed water and drainage water on sorghum plants. Irrigation with the Nile fresh water was used for **comparison**. Soil pH, EC, soluble cations both soluble sulphate and chloride and SAR significantly increased due to using mixed or drainage water. Higher values of plant height, dry weight/plant, weight of grains/panicle, 1000-grain weight and both grain and stalk yields, as well as N, P, K, Ca and K/Na ratio in sorghum leaves and grains were recorded for the plants irrigated with the Nile fresh water or supplied with potassium and or putrescine. Plants irrigated with drainage water without potassium or putrescine recorded the lowest values, except for the 1000-grain weight which was not affected by putrescine. Effect of putrescine was more pronounced under mixed or drainage water. The treatment of using mixed water+potassium chloride+putrescine resulted in sorghum yield almost equal to that irrigated with the Nile fresh water. Foliar spraying with potassium and putrescine might mitigate the adverse effect of using saline water for irrigation.[14]

Structure of Putrescine: Putrescine is a four-carbon alkane-alpha, omega-diamine. It is obtained by the breakdown of amino acids and is responsible for the foul odour of putrefying flesh. It has a role as a fundamental metabolite and an antioxidant. It is a conjugate base of a 1, 4-butanediammonium.

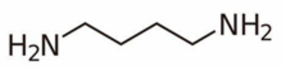


Figure-8: Structure.

Production of putrescine: Putrescine is produced on an industrial scale by hydrogenation of succinonitrile, which is produced by addition of hydrogen cyanide to acrylonitrile. Putrescine is reacted with adipic acid to yield the polyamide Nylon 46, which is marketed by DSM under the trade name Stanyl. Biotechnological production of putrescine from renewable feedstock is a promising alternative to the chemical synthesis. A metabolically engineered strain of *Escherichia coli* that produces putrescine at high titre in glucose mineral salts medium has been described.

Biochemistry of putrescine: Spermidine synthase uses Putrescine and S-adenosylmethioninamine (decarboxylated S-adenosyl methionine) to produce spermidine. Spermidine in turn is combined with another S-adenosylmethioninamine and gets converted to spermine.

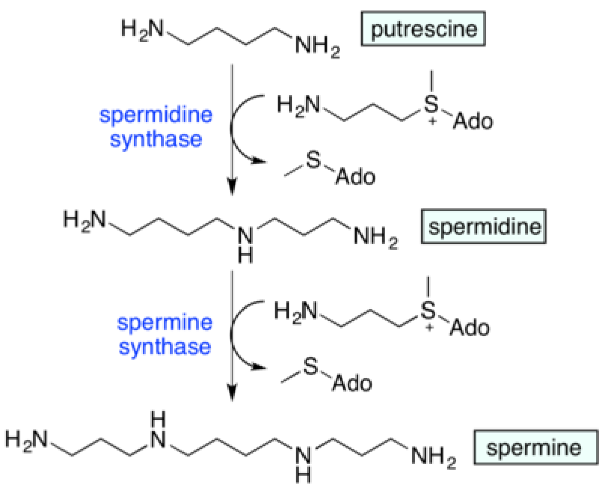


Figure-9: Biochemistry.

Putrescine is synthesized in small quantities by healthy living cells by the action of ornithine decarboxylase. Putrescine is synthesized biologically via two different pathways, both starting from arginine. In one pathway, arginine is converted into agmatine, with a reaction catalyzed by the enzyme arginine decarboxylase. (ADC); then agmatine is transformed into N-carbamoylputrescine by agmatine imino hydroxylase (AIH). Finally, N-carbamoylputrescine is converted into putrescine. In the second pathway, arginine is converted into ornithine and then ornithine is converted into putrescine by ornithine decarboxylase (ODC). The polyamines, of which putrescine is one of the simplest, appear to be growth factors necessary for cell division.[15]

Toxicity: Putrescine is toxic in large doses. When heated to decomposition, putrescine emits toxic fumes of NOx. **Uses:** The natural polyamines (putrescine) are ubiquitous low molecular weight aliphatic amines that play multifunctional roles in cell growth, differentiation, and survival. Polyamines are unique because of their flexible polycationic nature that allows them to bind electrostatically to negatively charged macromolecules including nucleic acids, acidic proteins, and membranes. Polyamines (putrescine) regulate important cellular processes, including cell proliferation and viability. Genetic evidence indicates that polyamines are required for optimal growth of bacteria and are essential for aerobic growth in yeast. The cellular functions of polyamines also include intestinal mucosal maturation and cell migration. Polyamines have been shown to influence transcription, RNA stabilization, and translational frame shifting.

CONCLUSION

Cadavers play an immense role in livelihood as we all, know that after a dead body kept for a longer period after decomposition then an obnoxious or foul-smelling gas liberated out from there, which is “Cadavers.” This study suggests that dissecting human cadavers has educational and tactile benefits and may play an important role in the early development of future healthcare providers’ relationships with their patients. This study also suggests that anatomy programs with human cadavers should hold a funeral service for the cadavers to give students closure. Medical practitioners, surgeons, anatomy teachers, and researchers in the anatomical field cannot avoid Cadavers if they wish to become competent professionals. They need Cadavers skills to assist them in performing safe and satisfactory practices during their professional careers. Thus, it is not reasonable to conclude that Cadavers is obsolete in medical training. Like other polyamines, Cadaverine influences growth in few cases. The few differential responses could be utilized for plants economical manipulations. Cadaverine presence in plant is scarce in general and under stresses specifically. The pathway of biosynthesis of Cadaverine established seems to be similar both in microbes and animals. Kamio demonstrated anaerobic bacteria contained with Cadaverine linked with peptidoglycan otherwise gene lacking for the rest of polyamines, this provided uniqueness to microbes. Cadaverine is having some unrelated influences on plant processes for instance, translocation of parquet in roots of intact maize seedlings, making a reason for screening of large plant species for their Cadaverine presence and its relevance. Putrescine gas is recommend to spraying sorghum plants with 2% potassium sulphate, and 10 uM Putrescine solution, twice on sorghum plants irrigated with mixed or drainage water to obtained sorghum production equal to the plants irrigated with fresh water.

Here, is in brief about the volatile diamino alkanes gases.

REFERENCES

1. Ludwig Brieger, "Weitere Untersuchungen über Ptomaine" [Further investigations into ptomaines] (Berlin, Germany: August Hirschwald), 1885; 43.
2. Fecker LF, Rügenhagen C, Berlin J. Increased production of cadaverine and anabasine in hairy root cultures of Nicotiana tabacum expressing a bacterial lysine decarboxylase gene. Plant Mol Biol., 1993; 23: 11–21.
3. Von Staden H: The discovery of the body: human dissection and its cultural contexts in ancient Greece. Yale J Biol Med., 1992; 65: 223–224.
4. Howe A, Campion P, Searle J, et al: New perspectives – approaches to medical education at four new UK medical schools. BMJ, 2004; 329: 327–331.
5. Rainsbury D, Barbour A, Mahadevan V: College launches national anatomy project. Ann R Coll Surg Engl, 2007; 89: 19.
6. Patel SB, Mauro D, Fenn J, Sharkey DR, et al: Is dissection the only way to learn anatomy? Thoughts from students at a non-dissecting-based medical school. Perspect Med Educ, 2015; 4: 259–260.
7. Ghosh SK. "Human cadaveric dissection: a historical account from ancient Greece to the modern era". “Anatomy & Cell Biology”, 2015; 48(3): 153–69.
8. Simpkins CA, Simpkins AM. "The Birth of a New Science". “Neuroscience for Clinicians”. New York, NY: Springer, 2013; 3–24.
9. Haglund, William. Forensic taphonomy: The Postmortem Fate of Human Remains. CRC Press, 1996; 100. ISBN 0-8493-9434-1.
10. Ludwig Brieger, "Weitere Untersuchungen über Ptomaine" [Further investigations into ptomaines] (Berlin, Germany: August Hirschwald, 1885: 39.
11. Kamhi, Ellen, Ph.D., RN, HNC. Alternative Medicine Magazine's Definitive Guide to Weight Loss. Celestial Arts, 2007; 14.
12. Izquierdo, C; Gomez-Tamayo, JC; Nebel, J-C; Pardo, L; Gonzalez, A. "Identifying human diamine sensors for death related putrescine and cadaverine molecules". PLOS Computational Biology, 2018; 14(1): e1005945.

13. Rainsbury D, Barbour A, Mahadevan V: College launches national anatomy project. Ann R Coll Surg Engl, 2007; 89: 19.
14. Til, H.P.; Falke, H.E.; Prinsen, M.K.; Willems, M.I. "Acute and subacute toxicity of tyramine, spermidine, spermine, putrescine and cadaverine in rats". Food and Chemical Toxicology, 1997; 35(3–4): 337–348.
15. Federico R, Angelini R, Cona A, Niglio A. Polyamine oxidase bound to cell walls from Zea mays seedlings. Phytochemistry, 1992; 31: 2955–7.