# Journal of Agricultural Sciences Research

# CONVULSIONS: SODIUM FLUOROACETATE: A BIBLIOGRAPHIC REVIEW

*Aline Beatriz Batista da Silva* http://lattes.cnpq.br/6050714955787882

*Edilson de Souza Paiva Júnior* http://lattes.cnpq.br/1720820810665497

*Carolina Menezes Suassuna de Souza* https://lattes.cnpq.br/8301358227006445

*Iago Carvalho Barbosa* http://lattes.cnpq.br/6504995465266487

*João Paulo de Lacerda Roberto* http://lattes.cnpq.br/3537838102515968

*Marianne Rachel Domiciano Dantas Martins* https://lattes.cnpq.br/1884130046756744

*Paulo Wbiratan Lopes da Costa* https://lattes.cnpq.br/8963125756244327



All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0). Abstract: The use of pesticides is worldwide, especially in the areas of agricultural production in order to combat living beings harmful to production. The review aims to make the availability of essential information for the research area, on sodium fluoroacetate or FAS. For the development of this literature review, work was carried out through bibliographic research in articles and books on the subject addressed, following the methodology of exploratory study. A search for the online browser was performed by articles that contained keywords such as "convulsions", and "sodium fluoroacetate". It was observed that the mechanism of action of this compound is based on the transformation of fluoroacetate fluoroacetate, causing toxic and lethal effect on the body. Clinical signs can take between 30 minutes to 2 hours and 30 minutes to appear and depending on the species there will be a symptomatological variation in the animal. The diagnosis is based on the patient's clinical history, and there may be scarcity of diagnostic methods because the signals are not so evident. Sodium fluoroacetate therapy is done by attempting to block fluoroocrate action in the body. It is concluded that FAS poisoning involves multiple systems, which can have serious clinical consequences. Multifatorial poisoning by FAS, brings together a complexity of objectives, from cellular metabolism, and the variation sensitivity dose-species.

**Keywords**: Compound 1080; convulsions; Sodium fluoroacetate.

# INTRODUCTION

Considering the amount of the use of prancidated products worldwide, Brazil is among the countries that consume the most pesticides both domestic and agricultural nature, as well as products of importance for public health (Pacheco 2009). Despite this too much use, the population is unaware of the consequences that they can generate and the toxicity for human, plant and animal health. Which leads to high rates of intoxications in humans, which according to the World Health Organization (WHO 2007), only 1 in 50 cases of intoxication is notified.

Pesticides are generally used in underdeveloped countries, but it is a practice worldwide. In the case of Brazil, no consistent legislation is presented that repair its impacts on health, and that control this use.

Federal Law No. 7,802 of 11.07.89, regulated through Decree No. 98,816, in its article 2, item I, defines the term pesticide as: "the products and components of physical, chemical or biological processes intended for use in the production, storage and processing of agricultural products, in pasture, protection of Native or implanted forests and other ecosystems and also in urban, water and industrial environments, whose purpose is to alter the composition of flora and fauna in order to preserve it from the harmful action of living beings considered harmful, as well as substances and products employed as defoliations, desiccants, stimulators and growth inhibitors. "

Amid the significance of pesticide products, we will have to present the toxic agent fluoroacetate sodium (FAS), its history, characteristics, mechanism of action, clinical signs, diagnostic and therapeutic methods, from the perspective of exposing the importance of knowledge of it Substance, which can be easily found naturally in toxic plants in Brazil, Australia and South Africa. Since this toxic agent causes irreversible damage to human and animal health.

It is observed that studies on sodium fluoracetate is little performed and its pharmacological action can lead to human and animal death, this work aimed to perform a bibliographic review about the sodium fluoracetate compound.

# MATERIALS AND METHODS

For the development of this literature review, work was carried out through bibliographic research in articles and books on the subject addressed, following the methodology of exploratory study. A search for the online browser was performed by articles that contained keywords such as "convulsions", and "sodium fluoroacetate". The most relevant articles were selected for the elaboration of this work, and from their references other relevant references were located. To obtain information on the subject, the exploratory reading method was followed (verification if the work is of interest to work); followed by selective reading (selection of parts of interest to the review): Record of information extracted from sources in a specific instrument (authors, vear, method, results and conclusions). In the end, the files selected to elaborate this review were organized and the data containing crucial information on sodium fluoroacetate. pesticides and seizures were inserted in this work.

# REVIEW OF LITERATURE HISTORY

Powerful substance, synthesized in the 1940s by the United States of America in order to control the proliferation of predators and rodents to protect its army, which later its use became by prohibited law in several countries, due to its complex toxicity and for having no odor or taste. In Brazil its use began in 1965, but with the high number of fatal accidents, in 1980 it was removed from the market, and can be used only in public health campaigns, and in 1982 it was prohibited its importation, production and marketing throughout the national territory (Spinosa et. Al., 2008). In Brazil, South Africa and Australia, the active substance of FAS is also found naturally in some toxic plants (Collicchio-Zuanaze, Sakate & Crocci, 2006).

#### SODIUM FLUOROACETATE

Also known as compound 1080, fluoroacetate or monofluoracetic acid, in Brazil its active ingredient can be found in the toxic plant *Palicourea marcgravil* ("vick or coffee "), one of the main toxic plants. As we can also find this substance in *Dichapetalum cysmosum* ("gifblaar"), South American plant and in the plants of the genre: *Gastrolobium e Oxylbium* commonly in Australia (Spinosa et. al., 2008).

# CHARACTERISTICS AND MECHANISM OF ACTION

Among the characteristics of the FAS, this substance comes into a decomposition process when exposed to temperatures above 110 ° C, being chemically stable by its connection between fluoride and carbon atoms. It is highly soluble in water, and respectively insoluble in organic solvents. (Osweiler, 1998).

The action of FAS on the body causes toxic effect through lethal synthesis. The fluorochetate fluoroacetate transformation, which occurs as follows: acetylcoenzyme binds to the FAS, forming the fluoroacetyl coenzyme A, where in the Krebs cycle will combine the oxaloacetate, transforming into fluorochetate. In turn, fluorocitrate will act competitively, blocking the action of sorbling, preventing the conversion of citrate to isochitrate, interrupting the citrus acid cycle or Krebs cycle. This way, citrate will accumulate in all tissues, especially in the CNS and myocardium, and to a lesser extent in the liver. Thus the citrate accumulated in the tissues will perform serum calcium cheering function, causing hypocalcemia (Collicchio-Zuanaze, Sakate & Crocci; 2006).

It can be seen that intoxication is not through fluoroacetate but by transforming the metabolite into fluorochratrate, being the intoxication by this substance called lethal synthesis (Spinosa et. Al., 2008).

#### **CLINICAL SIGNS**

Depending on the dose ingested, the clinical signs will appear from 30 minutes to 2 hours and 30 minutes, with symptomatological variation according to the species. They may have epigastric discomfort and vomiting are rare. (Spinosa et. Al., 2008). Seizure, auditory nystagmus, hallucinations, fasciculations, changes in sensitivity in the region of the face. These and other neurological signs appear gradually after a period of latency of several hours. Central nervous system excitement (CNS), progressing to widespread seizures. Severe neurological depression between or after seizure episodes may occur, but the death of respiratory failure is rare in humans with fluoroacetate intoxication. Cardiac rhythm disorder is common only after the seizure. Alternate pulse, long sequences of ectopic (often multifocal) and ventricular tachycardia beats can evolve into ventricular fibrillation and death (Informa-NET DTA).

#### **DIAGNOSTIC METHODS**

The diagnosis of FAS poisoning is usually performed through the animal's progressive medical history, highlighting the intake of the toxic agent, and observations of anatomopathological findings and clinical signs. It is worth noting that the signs are not so evident, with scarcity of specific laboratory methods for a peculiar diagnosis. (Chi; LIN; Chen, 1999; O'HAGAN, 2004)

According to Sakai; Miyahara (1981) The use of qualitative methodology is the easiest way, where they develop methods of tissue detection, soil samples, liquid baits, urine, blood containing fluoroachetic acid.

Quantitative analysis techniques happen through high efficiency liquid chromatography (HPLC) and gas chromatography (CG). Analysis by gas chromatography to identify FAS was developed through its determination as acid in aqueous solvents. (KIMBALL;

#### MISHALANIE, 1993)

From this perspective, differential diagnoses of FAS poisoning are performed for lead poisoning, stricnine, anticholinesterasics, pesticides. (O'HAGAN, 2004).

Few laboratories perform the analytical identification technique, and when the substrate is animal makes it even more difficult, as toxic tissues, such as liver and blood are low, as the hydrosolubility of the FAS is high, making the process difficult. (CUNHA, 2008)

Thus, Burger; Flecknell (1994) presents that so far there is no effective agent that reveals or prevents the effects of FAS on the respiratory system, making evolution normally fatal.

Toxicological analysis by FAS and toxic agent identification is indicated for a definitive diagnosis, but this quantitative analyzes of this toxic becomes difficult, as toxic waste from tissues are low by making the process difficult.

#### THERAPY

In order to avoid damage caused by intoxication by the sodium fluoroacetate agent, it must initially try to avoid fluorochetate action by blocking the Krebs cycle, or rapidly prevent fluorochetate fluoroacetate metabolization. In these composite poisoning that provides acetate ions such as acetamide or glycerol monoacetate, they have favorable results in intoxications. However, it has some contestations about its potentiality, especially about the SNC mechanism of action (Schvartsman, 1991).

According to Collicchio-Zuanaze, Sakate & Crocci (2006) through the oral pathway, 5 types of ionic exchange resins and additive charcoal for gastrointestinal detoxification, experimentally used in intoxicated rats, under which the use of cholespitol decreased to decreased Mortality, when there was administration within 30 minutes that was made intoxication. It can be seen that to obtain a favorable result, the as soon as possible medication must be administered after intoxication, as is the case with dog poisoning, managing glycerol monoacetate with dose on 100 mg/kg. 10% calcium glutamate is indicated as secondary treatment as it antagonizes hypocalcemia that the FAS causes. In cats, 10% calcium glucanate and sodium succinate is therapeutic protocol where it causes pH standardization, and ionized calcium and sodium bicarbonate efficiently reverse hypochocalcemia and acidosis. metabolic. (Collicchiozuanaze, 2002)

Thus, although in the literature there is some successful cases in treatment, an antidote was not discovered for monofluracetic, which has no success in treatment (symptomatic), where the animal can death quickly in less than 1 hour after Ingestion of this substance. (Spinosa et. Al., 2008).

#### FINAL CONSIDERATIONS

It is concluded that FAS poisoning involves multiple systems, which can have serious clinical consequences. Multifatorial poisoning by FAS, brings together a complexity of objectives, from cellular metabolism, and the variation sensitivity dose-species.

Realizing this, there are some therapeutic protocols for such poisoning, where it is necessary to re -establish the Krebs cycle in order to enable the continuity of oxidative metabolism of the organism.

The variety and severity that are presented by clinical signs proposes individual observation and sensitivity to exposure and ingestion of FAS, which the therapeutic protocols must be performed according to the individual response of the body, and the diagnosis of intoxication as fast possible. Which makes treatment against the toxic agent more effective.

It is worth noting that deepening for the therapeutic protocol of this toxic agent is necessary, as is also essential diagnostic methods in greater accuracy, in order to avoid the consequences that can lead to death by intoxication through FAS.

# REFERENCES

BURGER, I. H.; FLECKNELL, P. A. Poisoning. In: CHANDLER, E. A.; GASKELL, C. J.; GASKELL, R. M. Feline Medicine and therapeutics. 2 ed. NeW York: Blackwell Science, p. 656 – 677, 1994.

BRASIL. Lei Federal nº 7.802 de 11/07/1989. Dispõe sobre os agrotóxicos.

CHI, C. H.; LIN, T. K.; CHEN, K. W. Hemodynamic abnormalities in sodium monofluoroacetate intoxication. Human and Experimental Toxicology, v.18, p. 351 – 353, 1999.

COLLICCHIO-ZUANAZE, RC. Intoxicação por fluoroacetato de sódio: avaliações clinicas, hemogasométrica, eletrocardiográfica e da eficácia do gluconato de cálcio e succinato de sódio como protocolo terapêutico. Botucatu, 2002. 133p. Dissertação (mestrado)- Faculdade de Medicina Veterinária e Zootecnia, Universidade Estadual Paulista.

COLLICCHIO-ZUANAZE, RC; SAKATE, M., CROCCII, A., Variabilidade clinica na determinação da dose tóxica oral em intoxicação experimental por fluoroacetato de sódio em gatos. Braz. J. vet. Res. Anim. Sci, São Paulo,v.43, n.1, p.117-124, 2006.

CUNHA, L. C. da; Avaliação dos efeitos tóxicos da *Mascagnia* rígida em ratos. Estudo anatomopatológico. Comparação entre metodologias cromatográficas para detecção do fluoroacetato de sódio. Universidade de São Paulo. Faculdade de Medicina Veterinária e Zootecnia. Dissertação de Mestrado, p. 34 – 36, São Paulo, 2008.

INFORME-NET DTA. Contaminantes químicos/ intoxicação por substâncias químicas. Manual das doenças transmitidas por água e alimentos. Secretaria de Estado da Saúde de São Paulo Centro de Vigilância Epidemiológica - CVE Divisão de Doenças de Transmissão Hídrica e Alimentar. Acesso em 08/06/2014 as 22:43 min. ftp://ftp.cve.saude.sp.gov.br/doc\_tec/hidrica/ifnet\_ químicos.pdf

KIMBALL, B. A.; MISHALANIE, E. A. Gas chromatography determination of sodium monofluoroacetate as the free acid in an aqueous solvent. Journal Chromatography, v. 634, p. 289 – 296, 1993.

OSWEILER, G.D. Rodenticidas. In: OSWEILER, G.D. **Toxicologia Veterinária**, Artes Médicas, Porto Alegre, v.1, cap.22, p.300-26, 1998.

OMS-Organização Mundial da Saúde. Cuarto estúdio coordinado por la OMS sobre contaminantes orgânicos persistente em le leche materno, em colaboración com el Programa de las Naciones Unidas para el Medio Ambiente (PNUMA) : Guía para la el aboración de um protocolo nacional. Geneva; 2007.

O'HAGAN, B. J. Fluoroacetate poisoning in seven domestic dog. Australian Veterinary Journal, v.82, p. 756 - 758, 2004.

PACHECO, P. Brasil lidera uso mundial de agrotóxicos. O Estado de São Paulo. 2009 ago 07; Economia e Negócios. Acesso em 08/06/2014. https://www.estadao.com.br/economia/brasil-lidera-uso-mundial-de-agrotoxicos/

SAKAI, T. F.; MIYAHARA, T. Flourometric determination of monofluoroacetate acid. Eisei Kagaku, v. 27, p. 45 – 49, 1981.

SCHVARTSMAN, S. Intoxicações agudas. 4 ed. São Paulo: Sarvier, 1991. P.223-4.

SPINOSA, H. de S.; GÓRNIAK, S. L.; PALERMO-NETO, J. Toxicologia aplicada a medicina veterinária. 1ª edição. Barueri – SP: Editora Manole, 2008. 942p.