Therapeutic management of intoxication with sodium fluoracetate (matarratas guayaquil®) and sodium monoacetate (matarratas sicario®) in caninos, medellín, colombia (2015-2018)

Abstract
Report on the therapeutic management of intoxication with fluoracetate and sodium monoacetate in canines, in Medellin, Colombia, between the years 2015 to 2018. Thirty canine patients, who came to consultation with neurological symptoms, dysphoria and convulsion, of one hour of evolution, All the animals were in contact with sodium fluoracetate (Guayaquil® rat poison) or sodium monoacetate (Sicario® rat poison), orally. All the patients were evaluated in their physiological constants and neurological status, according to the Glasgow scale. Protocol was maintained until the absence of convulsive signs, dysphoria and delirium. Thirty patients survived intoxication, the average recovery was 3days, it was not possible to determine the presence of sequelae after intoxication, patients received medical control 20days later. Neurological sequelae could not be determined. Timely management of the toxic condition, with anticonvulsants, alkalizing solutions, calcium gluconate, glyceryl guayacolate and ethanol, proved to be effective strategies for the management of poisoning by sodium fluoracetate or sodium monoacetate.

Keywords: convulsion, delirium, rodenticides, toxic, calcium gluconate

Abbreviations: SAM, sodium monoacetate; SAF, sodium fluoracetate; ATP, adenylic triphosphate

Introduction
Sodium fluoracetate (SAF) or compound 1080 and sodium monoacetate (SAM), are well known in Colombia under the name of “Matarratas Guayaquil” and “Matarratas Sicario”; both are highly toxic rodenticides for all species.1–3 LD50 mg in dogs has been determined at 0.1-0.2mg/kg and in cats at 0.3-0.5mg/kg.4 In Colombia its use is prohibited, as in many countries of the world, but they are frequently used for the control of rodents or animals or pests.2,5 In countries such as Australia and New Zealand, its use is often described, for the control of Foxes and other species introduced to these countries, causing intoxication to domestic species.6 The characteristics of both is that it is a colorless toxic for sodium fluoracetate and bluish colored for sodium monoacetate, unsatisfactory, odorless Berrouet-Mejia et al.7 Goh et al.8 Isea et al.9 its chemical formula is FCH5O5N2, it is a white powder, in its pure form, that when diluted in water forms the well-known solution Berrouet-Mejia et al.7 they are also soluble in most organic solvents and non-combustible, which facilitates its dissemination and use Molina,8 as well as contaminating environments such as parks and green areas. The natural sources are plants such as: Acacia georginae, Dichapetalum toxicarum, Gastrolobium grandiflorum and Oxylobium parviflorum,2,7,9 all these plants present in the Americas and in other countries with. The mechanism of action of SAF and SAM in the organism is to inhibit the tricarboxylic acid cycle or Krebs cycle Dávila-Guajardo et al.10 which leads to a depletion of the Adenyl triphosphate (ATP).6,7 Normally AcetylCoA is converted to citrate by the enzyme citrate synthetase and then in CIS aconitato, by the action of the enzyme aconitas.1,2

SAF and SAM combine with AcetylCoA, forming fluorocacetyl-CoA Durango et al.11 the enzyme citrate synthetase is conjugated with this and with oxaloacetate, thus generating fluorocytate Berrouet-Mejia et al.2 Dávila-Guajardo et al.8 & Durango et al.11 this is not recognized by the aconitase enzyme, blocking the Krebs cycle.4,6,11 This blocking of the Krebs cycle was described by Peters, 1963 and is known as the Petears lethal synthesis.5,7 In this process, there is an accumulation of fluorocytate, which is not transformed into an isocyclic step in the generation of pyruvic acid.4,6 These alterations are responsible for tetanus contractures in several animal species, including canines, where this type of intoxication is quite frequent in the Colombian environment.1 In carnivorous species the acute toxic picture is characterized by rapid and dyspneic breathing, tremors that evolve to muscle spasms, and then move to a convulsive condition,4,6 these seizures are characterized by clonic movements -tonics, well described in the canine species Molina,4 which can differentiate them from epileptic canines especially. Nervous symptoms such as seizures appear rapidly within the beginning of the picture,4 then signs such as dysphoria, opisthotonos, delusions and excited states appear,1 which are often described by the owners as a patient’s state of madness.8

Later there is a severe depression and cardiovascular changes, with ventricular fibrillation Berrouet-Mejia et al.2 & Durango et al.11 Arrhythmias of the ventricular type are widely described, due to
alterations in the levels of calcium in blood, both SAF and SAM, cause severe hypocalcemia, in human patients the latter is considered to be the cause of death,1,2 while in the canine species in the Colombian environment, sometimes for veterinarians, this process is complex, since not all health centers have the equipment for early diagnosis of this condition, hence the canines mainly die from respiratory failure. No useful antidote is known in medical practice, with symptomatic support measures being the most important.5,6,10 It should be noted that the treatment of dogs intoxicated with both SAF and SAM is Little cash. It is effective in many cases, considering mortality rates at 90%.4,6,10 Some empirical treatments have been designed, but symptomatic treatment is always recommended, with management of circulation, breathing, airway (BCA) measures, induction of vomiting Dávila-Guajardo et al.4,19 use of chelators and adsorbents (activated charcoal), seizure control (Pentobarbital, Propofol, Etomidate and Alfaxalone), hypocalcemia and antiarrhythmic management.2,5 An antagonist drug is glyceryl monoacetate (Monoacetin®) as part of therapy for the treatment of both SAF and SAM, which behaves as a type of antidote for this condition, but is not available in South American countries and especially in Colombia.2,6,7 Some authors discuss its use, because they cause serious problems of hemolysis and pulmonary edema.12 Using ethanol for energy management of the patient to counteract toxicity in the Krebs cycle,1,2,4 the suggested dose varies from the concentration of ethanol, going from 1-5 ml/kg for 96% ethanol, up to 10ml/kg for 28% commercial ethanol.1 The diagnosis must be made by history (anamnesis), the data on the use of substances in baits such as “Matarratas Guayaquil®” or “Matarratas Sicario®” (Figure 1) are very important (it is important that from the clinical evaluation it differs from other intoxications such as those caused by strychnine and other stimulants of the central nervous system CNS), and must even be differentiated from infectious and metabolic diseases that compromise the CNS.7,10

Although the literature has described a group of methods for clinicians in human medicine for the diagnosis of SAF/SAM poisoning, such as: indirect measurement of the compound or its metabolites by various techniques, gas chromatography, liquid chromatography and capillary zone electrophoresis,2,6 the availability of these techniques in veterinary medicine in the Colombian environment are very limited, so they are considered only as theoretical references, although some veterinary clinics have been working with the use of measurement of lactate in blood, finding values above 20mmol/L in patients with poisoning by SAF or SAM, being a hypothesis that has yet to be proven and is that dogs that present seizure with lactate above 20mmol/L, They are intoxicated with SAF or SAM.

Materials and methods

The study was observational, prospective and descriptive, conducted on thirty canine patients who presented with poisoning with sodium fluoracetate (SAF) or sodium monoacetate (SAM) between January 2015 and January 2018, in several veterinary clinics in the city of Medellin Colombia. Thirty canine patients were evaluated, of which 10 were females and 20 males, of the breeds Cocker Spaniel 1, Beagle 3, French Bulldog 4, English Bulldog 2, Labrador Retriever 4, Golden Retriever 1, Mestizo 4, German Shepherd 1, Poodle 5, Pinscher 1, Pitbull 2, Pug 1, Schnauzer 1. All patients arrived at the clinic with neurological symptoms, subsequent to the consumption of sodium fluoracetate (Matarratas Guayaquil®) or sodium monoacetate (Matarratas Sicario®), verified by the presentation of the product by the owners and the history of the use of baits in the house (Figure 1). Patients were admitted to the emergency service of several veterinary clinics in Medellin, Antioquia, Colombia, with clinical signs of dysphoria, manifested by vocalization, delirium, incoordination, excitation and clonic tonic convulsions, as well as relaxation of sphincter, anal and bladder, patients They underwent neurological evaluation according to the Glasgow scale to assess the state of consciousness (Table 1).

### Table 1 Glasgow reference scale

| Glasgow modified scale | Points |
|------------------------|--------|
| Motor Activity         |        |
| Normal step, normal spinal reflexes |        |
| Hyperpnea, tetraparesis or decorticated activity | 6 |
| Recumbence with intermittent extensor rigidity | 5 |
| Recumbence with constant extensor rigidity | 4 |
| Recumbence with constant extensor rigidity and opisthotonus | 3 |
| Recumbence, muscular hypotonia, and depressed or absent spinal reflexes | 2 |
| Cranial reflexes       |        |
| Pupillary responses to light and normal oculocephalic reflexes |        |
| Slow pupillary responses to light, and reduced oculocephalic reflexes | 6 |
| Bilateral miosis with normal to reduced oculocephalic reflexes | 5 |
| Miotic pupils with oculocephalic reflexes reduced to absent | 4 |
| Irresponsible unilateral mydriasis with oculocephalic reflexes reduced to absent | 3 |
| Bilateral, irresponsible mydriasis with oculocephalic reflexes reduced to absent | 2 |
| Conscience level       |        |
| Occasional periods of alert and responsive to the environment |        |
| Depression or delirium, with inappropriate responses to the environment | 6 |
| Semicomatous, responsive to visual stimuli | 5 |
| Semicomatous, responsive to auditory stimuli | 4 |
| Semicomatous, responsive only to repeated noxious stimuli | 3 |
| Comatose, irresponsible to repeated noxious stimuli | 2 |
| Forecast               |        |
| Serious                | 3-8    |
| Poor to moderate       | 9-14   |
| Moderate to Good       | 15-18  |

The scale was evaluated every 12hours during the days of hospitalization. All the owners reported that the patients did not respond to the call and were unable to recognize the master. The group of animals received general clinical evaluation, with evaluation of the physiological constants, rectal temperature, femoral pulse, heart rate, respiratory rate, capillary refill time. This clinical evaluation was performed every 8 hours during the days of hospitalization. In addition, complete hemleucogram, creatinine, urea, alanine aminotransferase (ALT), alkaline phosphatase (ALP), Ionogram (Sodium, Chlorine, Calcium and Potassium) and sodium bicarbonate, taken in EDTA and dry, from the jugular vein and sent to reference laboratory. The patients were canalized in the external cephalic vein to lactate solution of ringer (Hartman), at a rate of 60ml/kg/hour.
then received for the control of seizures pentobarbital 10mg/kg endovenous (EV), every 12 hours, the duration depended if patients presented clonic upon awakening of barbiturate; if they had the clonic sign, they received a new dose of pentobarbital at 10mg/kg EV; This was also administered if neurological signs were present, such as convulsion, delirium, dysphoria and excitement. All the canines were intubated with tracheal tube according to the tracheal diameter and then received intravenously in continuous infusion: glyceryl guayacolate 100mg/kg, calcium gluconate 1mg/kg and ethanol 28% 10ml/kg for 24 consecutive hours. After the reporting of results they were submitted to basic acid balance therapy, for patients with sodium bicarbonate imbalance below 21 mEq/L, they received an infusion of sodium bicarbonate at a rate of 0.5mEq/kg for 24 hours.

**Figure 1** Commercial presentations of Matarratas Guayaquil® (Sodium Fluoracetate) and Sicario® Matarratas (Sodium Monoacetate) in Colombia, both products banned from sale.

The canines were evaluated every 2hours with complete clinical examination, especially evaluation of the nervous system, to determine the presence of convulsions, excitation, delirium and dysphoria, the absence of any neurological signs was considered as a parameter to suspend the therapy described above. Discharge was considered, 24hours after the absence of any nervous signs, without medication. All the patients were evaluated 15days after discharge, the Glasgow test, a general clinical and neurological examination, and all Glasgow values were considered 18 points normal.

**Results**

Thirty dogs were treated for poisoning by SAF or SAM, in different veterinary centers of Medellin, Colombia between 2015-2018, with acute convulsive symptoms, of which 10 were females (33.3%) and 20 males (66.6%), which were distributed in the following breeds: Cocker Spaniel 1 (3.3%), Beagle 3 (10%), French Bulldog 4 (13.3%), English Bulldog 2 (6.6%), Labrador Retriever 4 (13.3%), Golden Retriever 1 (3.3%), Mestizo 4 (13.3%), German Shepherd 1 (3.3%), Poodle 5 (16.6%), Pinscher 1 (3.3%), Pitbull 2 (6.6%), Pug 1 (3.3%), Schnauzer 1 (3.3%). All patients come with neurological signs ranging from excitation, delirium, dysphoria, vocalization, clonic tonic convulsion, dyspnea, polypnea, tachypnea, tachycardia, hyperthermia or hypothermia, sialorrhea, rinorrea, epifora, fasciculations, tremors (Table 2). Since vocalization, euphoria and tachycardia were the most frequent symptoms with 96.6% respectively, while stupor was the least frequent with 3.3%, the tonic clonic seizures typically described in the table only occurred in 28/30 canine evaluators. Regarding the assessment of the state of consciousness with the Glasgow scale, the following values were presented Table 3. The minimum value indicating a state of severity or critical state was 3, in five of the 30 dogs (16.6%) on day zero; while the mean value for the first day was 5.2, indicating that the patients arrived is a serious mental state, only one Beagle patient, came to consultation with Glasgow of 9, indicating a state of alteration from poor to moderate. In the second evaluation at 12 hours after the start of therapy, the Glasgow average went to a value of 7.2, considering that the patients were still in a serious condition; But 9 canines (30%), passed at 12hours to a state of poor alteration with Glasgow higher than 9. In the evaluation of the Glasgow scale at 24hours of treatment established, it was found that the average was 10.2, indicating a moderate state of alteration, and only one Labrador canine reached a state of 15 points indicating moderate alteration, at 12 hours later the average reaches 13.2 points, remaining in poor classification; but 8 canines reached Glasgow values higher than 15, considering moderate alterations; while four canines reached a state of normal mental evaluation with a value greater than 17 points. At 48hours of treatment the Glasgow average in the morning hours was 15.4 points, representing a state of moderate injury; where 15 canines had normal Glasgow evaluation status, superior to 17 points, without presenting neurological alterations; while 12hours later the evaluation of the patients increased the Glasgow average value to 16.9 points, with 70% of the patients recovered. At 72hours after establishing the therapeutic protocol described, an average of 17.7 Glasgow points was found, with a 96.6% positive response to therapy and a good Glasgow. Regarding the evaluation of the haemoleucogram (Table 4), the average of erythrocytes was 806693/ml, with a hematocrit 40.86% and hemoglobin 13.44g/dL, the parameters as leukocytes showed an average of 10 879/ml, lymphocytes 3 091 and platelets 308953/ml, considered normal in canines, the rest of the analytes in the blood count are within the normal parameters for the canine species, according to reference values Lathimer, Mahaffey & Prasser.**

| Sign                | Number of canines | Percentage (%) |
|---------------------|-------------------|----------------|
| Stupor              | 1                 | 3.3            |
| Euphoria            | 28                | 96.6           |
| Dysphoria           | 2                 | 6.6            |
| Vocalization        | 29                | 96.6           |
| Convulsion          | 28                | 93.3           |
| Tachypnea           | 20                | 66.6           |
| Tachycardia         | 29                | 96.6           |
| Polypnea            | 10                | 33.3           |
| Dyspnoea            | 15                | 50             |
| Hypothermia         | 5                 | 16.6           |
| Hyperthermia        | 25                | 83.3           |
| Sialorrhea          | 22                | 73.3           |
| Rinorrea            | 21                | 70             |
| Epifora             | 29                | 96.6           |
| Fasciculations      | 2                 | 6.6            |
| Sphincter relaxation| 5                 | 16.6           |
| Miosis              | 21                | 70             |
| Mydriasis           | 9                 | 30             |

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Table 3 Glasgow measurement scale, for each patient, during the days of hospitalization (times 1 and 2).

| Breed                    | Day 0 (0-24h) | Day 1 (24-48h) | Day 2 (48-72h) | Day 3 (72-96h) |
|--------------------------|---------------|----------------|----------------|----------------|
| Cocker spaniel (H)       | 4             | 5              | 7              | 9              |
| Beagle (M)               | 9             | 10             | 14             | 16             |
| Beagle (M)               | 6             | 8              | 13             | 17             |
| Beagle (H)               | 5             | 6              | 8              | 11             |
| French Bulldog (M)       | 3             | 3              | 5              | 8              |
| French Bulldog (M)       | 4             | 5              | 7              | 9              |
| French Bulldog (H)       | 5             | 8              | 9              | 12             |
| French Bulldog (H)       | 5             | 7              | 10             | 13             |
| English Bulldog (M)      | 8             | 9              | 14             | 16             |
| English Bulldog (M)      | 6             | 8              | 13             | 18             |
| Labrador Retriever (M)   | 7             | 10             | 15             | 18             |
| Labrador Retriever (M)   | 4             | 6              | 7              | 9              |
| Labrador Retriever (M)   | 6             | 9              | 13             | 15             |
| Labrador Retriever (H)   | 5             | 7              | 9              | 12             |
| Golden Retriever (M)     | 6             | 9              | 14             | 18             |
| Crossing (M)             | 5             | 9              | 12             | 16             |
| Crossing (M)             | 5             | 8              | 11             | 15             |
| Crossing (M)             | 6             | 11             | 13             | 17             |
| Crossing (H)             | 3             | 5              | 6              | 9              |
| German Shepherd (M)      | 8             | 12             | 15             | 17             |
| Poodle (M)               | 6             | 7              | 9              | 12             |
| Poodle (M)               | 3             | 4              | 5              | 8              |
| Poodle (M)               | 5             | 7              | 9              | 12             |
| Poodle (H)               | 3             | 6              | 8              | 9              |
| Poodle (H)               | 4             | 6              | 9              | 13             |
| Pinscher (H)             | 3             | 5              | 7              | 11             |
| Pitbull (M)              | 5             | 5              | 9              | 10             |
| Pitbull (M)              | 6             | 6              | 9              | 15             |
| Pug (M)                  | 6             | 9              | 13             | 15             |
| Schnauzer (H)            | 5             | 6              | 10             | 15             |

M, males; H, females

The canines that arrived with 3 points (critical state) according to the Glasgow scale, showed hemoconcentration, with a hematocrit >50% and hemoglobin between 19.6-21.8g/dL, respectively, which may indicate that the poisoning by SAF or SAM causes a severe dehydration in patients due to loss of water and electrolytes. With respect to the analysis of creatinine, urea, ALT and ALP, in the present case description the values for the canine species are considered normal as can be in Table 5, according to reference value taken from Lathimer, Mahaffey and Prasser, 2005. But due to the characteristics of the SAF-SAM intoxication, in which the hepatic metabolism and the glomerular filtration rate can be affected, the author suggests that for future reports the tests should be performed again several weeks later, as described by Dávila-Guajardo et al. 2005; Isea et al. 2003 The measurement of electrolytes, sodium, chlorine, potassium, calcium and sodium bicarbonate, showed the decrease in the values of potassium, calcium and sodium bicarbonate (Table 6). The average Sodium values in the present study was 148.13mEq/L (142-148mEq/L), being normal, only one patient had mild hyponatremia with 140mEq/L, a
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Table 4: Complete blood count for each patient at the time of entering the hospital.

| Breed                  | Erythrocytes/ml | Ht0 % | Hg gr/dL | VCM Fl | HCMC Pg | Leukocytes mil/µl | Neutrophils mil/µl | Eosinophils mil/µl | Lymphocytes mil/µl | Mono cytes mil/µl | Plasma proteins gr/Lt | Platelets/µl |
|------------------------|-----------------|-------|----------|--------|---------|-------------------|-------------------|-------------------|-------------------|-----------------|----------------------|-------------|
| Cocker Spaniel (H)     | 6790000         | 48.8  | 16.5     | 71.9   | 24.3    | 33.7              | 16390             | 13931             | 327               | 2130            | 0                    | 78          |
| Beagle (H)             | 751000          | 41.2  | 14.4     | 72.3   | 25.2    | 34.8              | 6230              | 4547              | 124               | 1432            | 0                    | 60          |
| Beagle (M)             | 8000000         | 40.2  | 13.4     | 71.9   | 23.9    | 34.9              | 9500              | 7600              | 475               | 1425            | 100                  | 65          |
| Beagle (M)             | 6450000         | 39.2  | 13.0     | 70.9   | 23.6    | 33.8              | 8972              | 6280              | 0                 | 66              | 0                    | 310000      |
| French Bulldog (H)    | 7300000         | 37.9  | 12.6     | 52.0   | 16.0    | 30.8              | 11910             | 4049              | 476               | 7384            | 0                    | 60          |
| French Bulldog (H)    | 9423000         | 41.2  | 13.7     | 61.9   | 20.6    | 31.6              | 10500             | 7875              | 100               | 2525            | 200                  | 71          |
| French Bulldog (M)    | 5456000         | 35.1  | 11.7     | 71.5   | 23.8    | 33.0              | 11250             | 8437              | 256               | 2557            | 0                    | 72          |
| French Bulldog (M)    | 6000000         | 38.5  | 12.8     | 61.9   | 20.6    | 34.2              | 12450             | 9960              | 300               | 2190            | 0                    | 68          |
| English Bulldog (M)   | 9070000         | 65.4  | 21.8     | 72.2   | 24      | 33.3              | 6230              | 5607              | 0                 | 373             | 0                    | 5567        |
| English Bulldog (M)   | 8945000         | 39.5  | 13.1     | 51.9   | 17.1    | 32.5              | 7800              | 4680              | 0                 | 3120            | 0                    | 30          |
| Labrador Retriever (M) | 8380000         | 57.5  | 19.6     | 68.6   | 23.3    | 34.0              | 12630             | 8083              | 505               | 4041            | 0                    | 70          |
| Labrador Retriever (H) | 9756000         | 48.5  | 16.1     | 68.9   | 22.9    | 33.0              | 13600             | 9520              | 200               | 3880            | 150                  | 71          |
| Labrador Retriever (M) | 9010000         | 54.2  | 18.0     | 71.1   | 23.7    | 35.0              | 14200             | 11076             | 156               | 2968            | 100                  | 75          |
| Labrador Retriever (M) | 10246000        | 50.2  | 16.7     | 70.5   | 23.5    | 36.4              | 11600             | 9164              | 230               | 2206            | 300                  | 65          |
| Golden Retriever (M)  | 10124000        | 46.2  | 15.4     | 66.9   | 22.3    | 32.8              | 10660             | 3160              | 542               | 6898            | 100                  | 66          |
| Crossing (H)          | 9442000         | 40.1  | 13.3     | 68.9   | 22.9    | 31.9              | 10700             | 7383              | 451               | 2866            | 0                    | 68          |
| Crossing (M)          | 7453000         | 38.2  | 12.7     | 62.9   | 20.9    | 32.7              | 11900             | 9520              | 300               | 2080            | 0                    | 71          |
| Crossing (M)          | 6623000         | 35.2  | 11.7     | 71.5   | 23.8    | 33.6              | 12900             | 9159              | 256               | 3485            | 250                  | 73          |
| Crossing (M)          | 9623000         | 39.4  | 13.1     | 71.1   | 23.7    | 34.0              | 10200             | 6936              | 453               | 2811            | 500                  | 70          |
| German Shepherd (M)   | 8856000         | 38.4  | 12.8     | 70.9   | 23.6    | 35.0              | 9800              | 6860              | 201               | 2739            | 230                  | 65          |
| Poodle (H)            | 5512000         | 32.2  | 10.7     | 73.4   | 24.4    | 35.4              | 8700              | 7000              | 156               | 1544            | 0                    | 66          |
| Poodle (H)            | 6721000         | 33.5  | 11.1     | 73.5   | 24.5    | 33.4              | 6450              | 4515              | 110               | 1825            | 0                    | 75          |
| Poodle (M)            | 10356000        | 46.2  | 15.4     | 72.5   | 24.1    | 32.1              | 9000              | 6480              | 50                | 2470            | 660                  | 76          |
| Poodle (M)            | 11000000        | 44.5  | 14.8     | 70.0   | 23.3    | 30.2              | 10000             | 7500              | 0                 | 2500            | 0                    | 72          |

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Table 5: Creatinine, Urea, ALT and ALP blood values for patients during the first 24 hours of treatment

| Breed        | Creatinine U/L | Urea mg/dL | ALT mg/dL | ALP mg/dL |
|--------------|----------------|------------|-----------|-----------|
| Cocker Spaniel (H) | 0.86          | 14.72      | 36.50     | 60.03     |
| Beagle (H)   | 0.90           | 17.56      | 33.16     | 52.08     |
| Beagle (M)   | 0.92           | 16.25      | 31.00     | 45.75     |
| Beagle (M)   | 1.50           | 15.70      | 55.41     | 48.10     |
| French Bulldog (H) | 1.45       | 20.21      | 49.55     | 55.53     |
| French Bulldog (H) | 0.87       | 14.73      | 55.12     | 60.12     |
| French Bulldog (M) | 1.02       | 15.00      | 51.23     | 55.64     |
| French Bulldog (M) | 1.12       | 15.60      | 52.35     | 45.89     |
| English Bulldog | 0.56         | 13.80      | 50.32     | 61.32     |
| Golden Retriever | 1.2          | 18.23      | 56.58     | 59.12     |
| Labrador Retriever (H) | 0.87       | 14.23      | 45.89     | 55.78     |
| Labrador Retriever (M) | 0.78       | 14.80      | 36.50     | 60.03     |
| Labrador Retriever (M) | 1.03       | 16.56      | 33.16     | 52.08     |
| Labrador Retriever (M) | 1.30       | 14.25      | 31.00     | 45.75     |
| Crossing (H) | 1.46           | 13.70      | 55.41     | 48.10     |
| Crossing (M) | 1.50           | 21.21      | 49.25     | 55.53     |
| Crossing (M) | 0.89           | 14.89      | 45.15     | 59.12     |
| Crossing (M) | 0.85           | 15.23      | 50.29     | 54.64     |
| German shepherd | 0.87         | 14.60      | 52.35     | 45.89     |
| Poodle (H)   | 0.99           | 13.80      | 50.32     | 61.32     |
| Poodle (H)   | 0.92           | 18.23      | 56.58     | 59.12     |
| Poodle (M)   | 0.78           | 14.23      | 45.00     | 54.78     |
| Poodle (M)   | 0.85           | 12.36      | 56.89     | 65.23     |
| Pitbull (M)  | 0.92           | 16.45      | 45.63     | 70.12     |
| Pitbull (M)  | 1.03           | 12.56      | 55.33     | 45.85     |
| Pinscher (H) | 1.45           | 18.45      | 66.2      | 91.2      |
| Pug (M)      | 1.23           | 16.23      | 45.2      | 89.45     |
| Schnauzer (H) | 1.13          | 18.41      | 45.66     | 69.68     |

M: male; H: female.
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Table 6 | Ionogram values for patients: Sodium, Chlorine, Potassium and Sodium Bicarbonate and GAP Anion in the first 24 hours

| Breed                  | Na⁺ mEq/L | Cl⁻ mEq/L | K⁺ mEq/L | NaHCO₃ mEq/L | Ca⁺ mEq/L | GAP mEq/L |
|------------------------|-----------|-----------|----------|--------------|-----------|-----------|
| Cocker Spaniel (H)     | 145       | 110       | 4        | 20           | 1         | 19        |
| Beagle (H)             | 146       | 106       | 3        | 19           | 2         | 14        |
| Beagle (M)             | 144       | 111       | 5        | 21           | 1         | 17        |
| Beagle (M)             | 150       | 108       | 6        | 22           | 2         | 26        |
| French Bulldog (H)     | 149       | 110       | 3        | 18           | 2         | 24        |
| French Bulldog (H)     | 148       | 113       | 2        | 16           | 1         | 21        |
| French Bulldog M       | 152       | 105       | 4        | 20           | 2         | 31        |
| French Bulldog M       | 153       | 113       | 3        | 21           | 2         | 22        |
| English Bulldog        | 147       | 119       | 2        | 22           | 2         | 8         |
| Golden Retriever       | 148       | 125       | 3        | 17           | 1         | 9         |
| Labrador Retriever (H) | 153       | 105       | 5        | 14           | 4         | 39        |
| Labrador Retriever (M) | 155       | 110       | 6        | 13           | 2         | 38        |
| Labrador Retriever (M) | 156       | 108       | 3        | 20           | 1         | 31        |
| Labrador Retriever (H) | 149       | 104       | 4        | 21           | 2         | 28        |
| Crossing (H)           | 147       | 103       | 4        | 24           | 3         | 27        |
| Crossing (M)           | 146       | 111       | 3        | 19           | 2         | 19        |
| Crossing (M)           | 142       | 108       | 5        | 18           | 1         | 21        |
| Crossing (M)           | 154       | 112       | 3        | 17           | 1         | 28        |
| German Shepherd        | 150       | 101       | 5        | 15           | 1         | 39        |
| Poodle (H)             | 151       | 100       | 6        | 12           | 1         | 45        |
| Poodle (H)             | 148       | 109       | 7        | 21           | 1         | 25        |
| Poodle (M)             | 146       | 108       | 6        | 19           | 1         | 25        |
| Poodle (M)             | 145       | 115       | 8        | 17           | 2         | 21        |
| Poodle (M)             | 143       | 120       | 8        | 15           | 3         | 16        |
| Pitbull (M)            | 140       | 123       | 4        | 16           | 2         | 5         |
| Pitbull (M)            | 146       | 125       | 5        | 18           | 2         | 8         |
| Pinscher (H)           | 155       | 124       | 3        | 21           | 1         | 13        |
| Pug (M)                | 145       | 110       | 2        | 22           | 2         | 15        |
| Schnauzer (H)          | 143       | 102       | 3        | 20           | 3         | 24        |

M, male; H, female.

Although the average value of Potassium was 4.31 mEq/L, considered normal 12 dogs (40%), they presented hypokalemia, with values below 3 mEq/L, among which three were female French Bulldogs, followed by two mestizos. Calcium presented an average of 1.79 mEq/L (9.8 mEq/L), this represented in 100% of the patients, all the canines admitted with severe hypocalcemia, and 40% were in a state of severe hypocalcemia with average Calcium of 1 mEq/L; as for sodium bicarbonate, the average value is 18.55 mEq/L (24 mEq/L) indicating a possible metabolic acidosis; 100% of the specimens arrived with Sodium Bicarbonate below 20 mEq/L, with the value of 12 mEq/L being the most extreme in a female Poodle. Regarding the average values of the GAP anion, which was 23.03 mEq/L (10-25 mEq/L), they are within the normal range for the canine species, 17 canines 56.66%, presented GAP anion below 25 mEq/L, indicating that several patients were admitted to severe metabolic acidosis.

Discussion

Sodium Fluoracetate (Matarratas Guayaquil®) and Sodium Monoacetate (Matarratas Sicario®) poisoning are very frequent in Colombia and especially in large cities, although there is no frequency or prevalence in the Colombian environment, it is widely described by veterinarians dedicated to small animals, as well as emergency centers in human medicine, where this intoxication is well described Molina, but the diagnosis remains a challenge, due to the impossibility of performing tests to detect the agent, make
the anamnesis and the presence of the product, the only reference of etiology of the present descriptive article, in which 30 canines were in contact with both Matarratas Guayaquil® and Matarratas Sicario®. The symptoms and signs coincide with those described by several authors, for this intoxication,6,8 the symptoms described, may have digestive component such as: vomiting, diarrhea, tenesmus, sialorrhea and hypermotility Dávila-Guajardo et al.,10 where the present sialorrhea presented 73.3% of the canines, which could be similar to the symptoms caused by other toxins such as the acetylcholinesterase inhibitors Córdoba,7 frequently used for the control of ectoparasites and as baits for rodents, but the concomitant absence of fasciculations, tremors and non-reactive miosis, rule out this possibility, since only 6.6% of canines showed fasciculations as a clinical sign and 70% miosis, as indicated by the symptoms neuromuscular with tremors, fasciculations, motor hyperactivity, pleja, paresis and spasms are frequent also in the intoxication with SAF or SAM Berrouet-Mejia et al.,2 Flem ing & Thompson,6 O’Hagan1 these signs are present above 90% of poisonings with organophosphates, carbamates, strychnine and pyrethrins-pyrethroids (Córdoba 2001), but the absence of information on the use of these substances in the present study indicate that the The cause of these signs is the use of SAF or SAM.

The neurological syndrome, which begins with an evident state of hyper-excitation Isea et al.,1 vocalization: howls and / barks, as if the animal will present a state of intense pain Isea et al.,1 dysphoria Berrouet-Mejia et al.,2 which in canines is observed, with a dog running desperate, untimely and with no recognition of the owner, they are almost pathognomonic of SAF or SAM poisoning Isea et al.,1 O’Hagan2 In the present study, these signs represent 96.6% of the manifestations shown by the canines, in addition the presence of convulsions as one of the typical signs of the picture, with movements of the clonic, repetitive and opisthotonic type, has been described by several authors. For humans as for animals Berrouet-Mejia et al.,1 Eason & Turck,9 O Hagan,19 which in the present case are 93.3% of the description, the union of both components of the neurological syndrome indicate that 100% of canines had contact with SAF or SAM. And as described previously, although the identification of the toxicity is fundamental for the diagnosis, particularly when there is no history of toxic exposure. Toxic or no access to the original source O’Hagan,7 for sodium fluoroacetate can be made on the basis of characteristic clinical signs, described by several authors in the dog and the history of exposure can be considered sufficiently compatible with the toxic picture of SAF.1,2,7 Conducting or confirming the diagnosis of sodium fluoroacetate poisoning is difficult; methods to determine fluoroacetic acid, sodium fluoroacetate or sodium monoacetate in biological tissues involve slow extraction procedures, low recovery rates and/or low selectivity.1 The methods for clinicians described indirectly, for the diagnosis of SAF or SAM are: gas chromatography, liquid chromatography and capillary zone electrophoresis,2,8 the availability of these techniques in Veterinary medicine in Colombia, are scarce for this reason, the confirmation of the poisoning by Guayaquil® killings and Sicario® killings in the present study could not be developed. In the analysis of the haemolucogram, it could not be determined alteration in the red or white cells by action of SAF or SAM, similar to that described by other authors.2,3,10 only some canines, the Glasgow scale of 3, in critical condition showed hemoconcentration, possibly due to the severe state of dehydration and metabolic acidosis caused by the tox. The other variables were normal; there was no alteration in the rest of the blood lines in any of the patients of the present description. The creatinine, urea, ALT and ALP analytes were normal for the five patients, so it can indicate that the acute poisoning with SAF or SAM, does not cause initial liver or kidney damage, but it is important to clarify that these tests should have been repeated once the patient recovered the normal state of consciousness and was discharged, to determine a possible renal or hepatic sequela. This was described by other authors during the necropsy of a patient intoxicated with SAF.5,10

The SAF or SAM causes a severe metabolic acid metabolism in the intoxicated patient. For this reason, the use of alkalizing solutions such as lactate ringer (Hartman) or Pizarro Solution (Solution 90®, Corpaul©, Medellín, Colombia) is considered as the indicated solution.2,6 It is important to note that Sodium Bicarbonate can be added, at a rate of 8-12mg/kg every 8hours Molina,21 until reaching a blood value of 24mEq/L, in the present study. The dose 0.5mEq/ kg/24hours in continuous infusion, the use of Hartman and sodium bicarbonate in the present study was sufficient for 24hours to reduce the signs of acidosis, in all patients. In the present description it is considered that it should be important to evaluate for the future the measurement of arterial gases and lactate to confirm the state of metabolic acidosis of the specimens, as described by several authors.2 Electrolyte imbalance is well documented for SAF or SAM, the presence of hypocalcemia and hypokalemia has been demonstrated in the canine species.6,9,10 In humans, this phenomenon has been described frequently, in addition to the arrhythmic states produced by this imbalance.2,12 In all the patients a severe state of hypocalcemia was found with Calcium levels below 5mEq/L (average 1.79mEq/L), which corroborates the data found by the authors mentioned, that both SAF and SAM, cause deadly hypocalcemia. Regarding potassium, it was found that 12 of the 30 patients showed hypokalemia, which has been documented by other authors.1,2,11 Evidently its start is missing bring severe cardiovascular consequences, especially induce cardiac arrest, for this reason the use of crystalloids with high content of Potassium Chloride as Hartman and Solution 90®, are indicated, because they provide 4mEq/L of Potassium and 3mEq/L of Calcium and 20 mEq/L of Potassium (Solution 908©) respectively, in addition to the use of Calcium Gluconate 1mg/kg in constant infusion, allowed to resolve the imbalance and guaranteed the improvement of the patient.6 The other electrolytes were found within the normal values for the canine species, for which it can be deduced that Calcium and Potassium are the two ions, involved in the pathological processes of SAF or SAM poisoning. It is also important to mention that The muscular signs of this intoxication, presenting tremors, fasciculations, spasms and tetanias, are recommended to be managed with non-nicotinic muscle relaxants such as glyceryl guaiacose at a dose of 110mg/kg in constant infusion Plumbs,24 the mechanism of action is inhibition of intercalary motor fibers in the CNS Goodman et al.14 it has been demonstrated that glyceryl guayacolate makes voluntary striated muscle relaxation, lowering the excitatory threshold and potentiating the effect of barbiturates Plumbs,21 which was demonstrated in patients with muscle relaxation, total absence of tremors, spasms and fasciculations, during the administration of the constant infusion of glyceryl guayacolate. The control of clonic tonic seizures in all patients of the present review, is effective with the use of a barbiturate such as pentobarbital, which is a GABA agonist, with opening of the channels of chloride, decreasing the excitability of the membrane.17,18 which is evident in all patients. In addition to the energy imbalance caused

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by SAF, it is important to determine that the alteration in the chlorine channels, as well as in the phenomena of depolarization and neuronal depolarization, are totally altered, hence the use of barbiturates as an excitatory control mechanism.4,5 is well-founded. For the author, the use of other GABA agonists, such as benzodiazepines, is impractical, because after their use, patients persist in the convulsive symptoms, as was described by Dávila-Guajardo et ál.6 for this report case, pentobarbital is the best anticonvulsive option, also described by other authors.7 With regard to the treatment of poisoning by SAF or SAM it should be noted that to date there is no specific antidote for this toxic, so the treatment is based on general decontamination measures: gastric lavage (recommended up to one hour after ingestion), activated and cathartic charcoal as well as the management of the symptoms or complications presented by the patient. In the therapy, two experimental options for the treatment of SAF intoxication have been described and used: glyceryl monoacetate and ethanol. Glyceryl monoacetate (Monoacetin®, not available in Colombia) was the most used, but its administration produced pulmonary edema and haemolysis as side effects in humans, so its use was abandoned, given the lack of safety and evidence of effectiveness.1,2,6,7 The efficacy of ethanol in the treatment based on clinical findings in species such as canines, allowed that the use will increase in the human species.2,3 There are several reports reports where the use of ethanol in SAF intoxication, that only support therapy.10 The ethanol protocol in SAF or SAM poisoning can be oral, by nasogastric or orogastric and venous tube.

The oral route is administered 28% ethanol at a rate of 0.3-0.5cc/kg/h for 24hours Berrouet-Mejia et al.2 Córdoba1 in humans, in the canine species the use of ethanol has been reported. Ratio of 5-10ml/kg in continuous infusion.3 For the author of the present report a dose of 10ml/kg in 24hours, has proved to be efficient in practice to maintain energy levels in the patient Molina,4 which agrees with the experience of 0.5-1 ml/kg/hour in human patients described in the university hospital San Vicente de Paul, Medellín, Colombia.2,3 The rationale for the use of ethanol in SAF poisoning is based on the depletion of the intermediary of the Krebs cycle, citrate, which was converted into fluorocitrate, the oxidative metabolism of ethanol, acetate form, which is transformed into AcetylCoA, this process occurs during 24-36 hours Berrouet-Mejia et ál.4 Eason & Turk14 this explains why patients began to improve after 36 hours, this process guarantees the supply of precursors to the Krebs cycle, this is how aconitase does not block,2,3 by absence ia of substrate, and the energy cycle continues, generating new acetylCoA, as a new substrate. Therefore, the supply of ethanol in constant infusion during the first 24-36hours is fundamental, as was described in this report.

Conclusion
The difficulty for laboratory diagnosis of SAF intoxication in the Colombian environment, for veterinary medicine remains a limitation in the clinic of small animals, leading to the envelope or sub-diagnosis of this important substance in Colombia, only the clinical history, exposure, symptoms and signs allow us to reach a presumptive diagnosis of the problem. In addition to the absence of a proven antidote for canine poisoning, the use of conservative measures, stabilization of the patient, the use of pentobarbital, glyceryl guaiacolate, calcium gluconate, buffer solutions (Hartman) and ethanol, proved to be a good strategy to ensure patient survival, because sodium fluoracetate poisoning is a potentially fatal event.

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Conflict of interest
The authors declare that there is no conflict of interest.

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