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CASE STUDY OF A SEVERELY INFECTED DOG WITH *SARCOPTES SCABIEI* MITES AND THE MATHEMATICAL STUDY OF THE INTERACTIONS BETWEEN MITES AND HOST

BY

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Abstract. Sarcoptic mange in dog represents a parasitic skin disease, caused by the *Sarcoptes scabiei* mite, characterized by intense pruritus, alopecia, crusts and scales. It is frecquently a problem in shelters or in big communities of animals, because it is a highly contagious disease.

Our research consists of a case study of a dog, which was severely affected by sarcoptic mange.

Clinical evaluation of the characteristic clinical signs present in sarcoptic mange in dogs was performed and scored at different time points (days – D) and photos of the dog were taken (0, D14, D28, D56). The treatment consisted in afoxolaner, which was given at D0 and D28. We then compared the evolution of the clinical score after the first and second treatment, which proved a good efficacy of the molecule chosen.

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Furthermore, we studied the dynamics of the complex system mite-canine organism through the evolution of the disease and until the curing of the animal.

Keywords: mange; dog; clinical score; afoxolaner; complex system; mite-canine organism.

1. Introduction

The disease caused by *Sarcoptes scabiei* in humans, is known to mankind since ancient times, with one of the oldest mentions in the Bible, where priests were supposed to differentiate scabies from leprosy (Roncalli, 1987).

S. scabiei is an arthropod, from the class Arachnida, order Sarcoptiformes, family Sarcoptidae (Zhang, 2011). It is a pathogenic burrowing mite that affects the skin of a wide range of animals and also humans. Generally, the disease is called scabies in humans and mange in animals.

Concerning the veterinary importance, sarcoptic mange in farm animals produces great economical losses, since it spreads rapidly in communities of animals. It represents a problem also in communities of wild animals, where several outbreaks of mange have been reported as epizooties, with great loss of individuals (Pence and Ueckermann, 2002). Furthermore, companion animals are also severely affected by the disease.

As far as the public health aspect in humans is concerned, scabies is one of the commonest and most frequent skin infection worldwide and is estimated to affect between 177 and 237 million people globally at any time (Vos *et al.*, 2016).

S. scabiei adults have a characteristic oval, ventrally flattened and dorsally convex body. Larvae have 6 legs,while nymphs and adults have 8 legs, with suckers present on legs I and II in both sexes and on legs IV only in males. The suckers help the mite grip the substrate as it moves. The female size is 315 to 470 µm long by 225–345 µm wide, and the male size is 205 to 245 µm long by 145–170 µm wide, around two-thirds the size of the female (Cosoroabă, 2014). Both females and males have short legs, with the last 2 pairs not passing beyond the body margin.

Regarding the life cycle of *S. scabiei*, it is important to note that it takes place entirely on the skin of animal. It starts with the coupling of the adult male and female on skin surface and after mating, the male will die and the female will begin creating her tunnel into the stratum corneum of the skin, digging with a rate of 2-3 mm/day and laying 1-3 eggs per day in the burrows for about 2 months. Each female has its own tunnel, where only her, the eggs and faeces are present (Taylor *et al*., 2016). This tunnel was studied in humans through entodermoscopy, and proved to be complex and even more elaborate than it was thought before, being composed of 3 parts: Head (where the adult can be found), Body (where the eggs and faeces are deposited) and Tail (incomplete

structure without a roof) which represent a new concept called the Mite Gallery Unit. This concept takes into consideration the behaviour of the burrowing mite correlated with his interactions with the human skin, bringing some new perspectives in the study of the *S. scabiei* (Scanni, 2019).

The eggs will hatch into six-legged larvae within 2 to 3 days. The larvae will go to the surface of the skin and transform into octopod protonymphs in 3-4 days and into tritonymphs in 2-3 days and then moult into either males or females. The entire process from egg to adult takes about 14 days, more specifically, 10.1−13.2 days for the male and 9.9−13.0 days for the female of *S. scabiei* var. canis (Arlian and Vyszenski-Moher, 1988). All the stages of *S. scabiei* can penetrate the skin surface, consume lysed cells and tissue fluid that oozes when digging the burrows (Hengge *et al*., 2006).

There is a big debate on the idea if the genus *S. scabiei* contains one species with several varieties or different species, because strains from different hosts are morphologically similar. Most scientists agree with Fain that the genus Sarcoptes contains only one valid, but variable species with numerous varieties (Fain, 1968; Fain, 1978). Fain described over 15 different varieties of *S. scabiei* mites from different hosts. Each variety is adapted to a specific host or a small number of related hosts and there is little evidence of interbreeding between varieties or strains (Neveu-Lemaire, 1938). Human contamination cases following contact with an infected animal have been observed, but the disease is self-limiting, with no evidence of reproduction on the accidental host (Morsy *et al*., 1994).

Sarcoptic mange is a very contagious disease and can be spread through direct contact between individuals, or indirectly, through fomites (Burkhart *et al*., 2000). The indirect transmission is important to be taken into consideration, since all life stages of S. scabiei leave the burrow and can accidently fall of the host (Arlian *et al*., 1984).

In dogs, sarcoptic mange presents the following almost constant clinical signs: diffuse or localized alopecia, pruritus, presence of crusts. The lesions will be more visible on the head (the muzzle, the ears), the abdomen, the feet, the elbows, the hocks. They will be erythematous, with papules and vesicles with a grey-yellow crust that will form the "mangy buttons" that can be observed when touching (Miller *et al*., 2012).

The diagnosis of sarcoptic mange is made by identification of adults, larvae, eggs or feces of *S. scabiei* mites, through microscopic examination of the skin scrapings collected from several areas that contain lesions, especially crusts.

Concerning the treatment of the disease in dog, the authorized molecules in the European Union are as follows: imidacloprid/moxidectin, selamectin, sarolaner and the newly approved afoxolaner and afoxolaner/milbemycin oxime. The last 3 molecules are from the isoxazoline family, a new chemical class of acaricides and insecticides, introduced in the 2000s, that have proven efficacy against some ectoparasites. The use of

afoxolaner in curing sarcoptic mange in dogs has been studied before, through 2 studies that showed a great efficacy of the product following two administrations at 28 days interval (Beugnet *et al*., 2016; Hampel *et al*., 2018).

Another interesting aspect to be taken into consideration is the interaction between the *S. scabiei* mite and the host, in our case, the dog. Determinism does not necessarly imply regulated behavior (periodical evolutions and self-structures) or predictability in dynamics of the complex system mite-canine organism. In the linear analysis focused on biophysics of the complex system mite- canine organism, unlimited predictability was an automatic quality of the system. Development of non-linear analysis and the discovery of laws regarding chaotic behavior of the complex system mite-canine organism, demonstrated that not only does the reductionist analysis method, on which the entirety of biophysics was grounded so far, has limited applicability, but also that unlimited predictability is not an attribute of the complex system mite- canine organism, but an expected consequence of simplifying its description through linear analysis (Badii and Politi, 1997; Cristescu, 2008; Mitchell, 2009).

The chaotic and non-linear nature of the complex system mite- canine organism is both structural and functional, and the interactions between structural units of the complex system mite- canine organism determine reciprocal conditionings of the types microscopic-macroscopic, local-global, individual-collective etc. Within this theoretical framework, the universality of the laws describing the complex system mite- canine organism dynamics becomes obvious and must be seen in the used mathematical procedures. There is increasing discussion regarding graphic implementations in the description of complex system mite- canine organism dynamics (Badii and Politi, 1997; Cristescu, 2008; Mandelbrot, 1983). Usually, models used to describe complex system mite- canine organism dynamics are based on the uncertain hypothesis that the variables describing it are differentiable (Badii and Politi, 1997; Cristescu, 2008; Mandelbrot, 1983; Nottale, 2001). The success of these models must be understood sequentially on domains in which the differentiability is still valid. The differential procedures however "suffer" when describing processes regarding complex system mite- canine organism which imply nonlinearity and chaos (which is usually the case).

The aim of this study is to present the evolution of clinical signs of sarcoptic mange in dog, throughout the treatment with afoxolaner. Furthermore, the study will focus on investigating the link and the nature of the complex system mite-canine organism, from a mathematical point a view.

2. Material and Methods

In this study we evaluated the case of one dog, which presented typical signs of sarcoptic mange (alopecia, crusts, pruritus).

For confirmation of the diagnosis, skin scrapings were made, from different body parts, including the head, the trunk and the legs. The scrapings were performed using a sterile scalpel until oozing blood resulted and then put on a slide, spread in mineral oil and covered with a coverslip. The slides were then examined at the microscope with 10X objective. The samples were considered positive if either adult, larvae, eggs or faces of *S. scabiei* mites were present. This procedure was done at D0, D28 and D56.

A general health exam was conducted at enrolment in the study, at D0.

The dermatological exam included the assessment of an original clinical score, designed for pigs infected with *S. scabiei*, but adapted for dogs (Bernigaud *et al*., 2016). The grades were from 0 to 4, with 4 being the most severe, given to some characteristic signs that appear in mange in dogs such as: the skin area affected by sarcoptic mange, alopecia, skin erythema, and crusts or scales. These signs were evaluated on different parts of the body (head, trunk, legs and tail), adding in a total clinical score that could be between 0 and 60. This score was calculated at D0, D14, D28, D56.

Regarding the treatment protocol, we used the orally administrated product NexGard® (afoxolaner), according to commercial registration labeling, taking into account the weight of the animal, which resulted in a dose between 2.7 and 6.9 mg/kg. The treatment was administrated at D0 and D28.

3. Results and Discussions

The experimental unit was the individual dog. The dog that we studied was a 2 year old male stray dog from Vrancea county, with an unknown history. The general aspect of the dog was characteristic for a severely, generalized sarcoptic mange. The dog, named Sniff, was hospitalized in our clinic for the whole period of treatment and 2 months after, until his coat was fully recovered (Fig. 1).

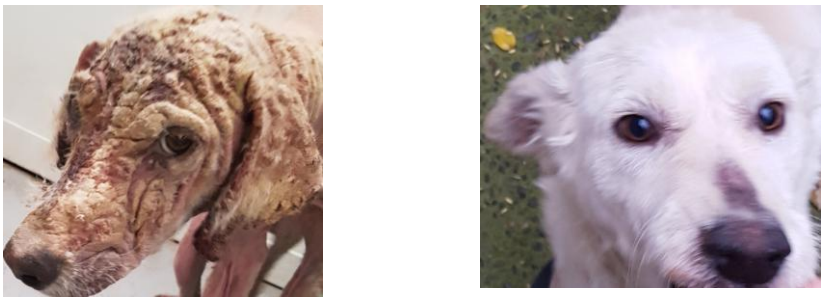
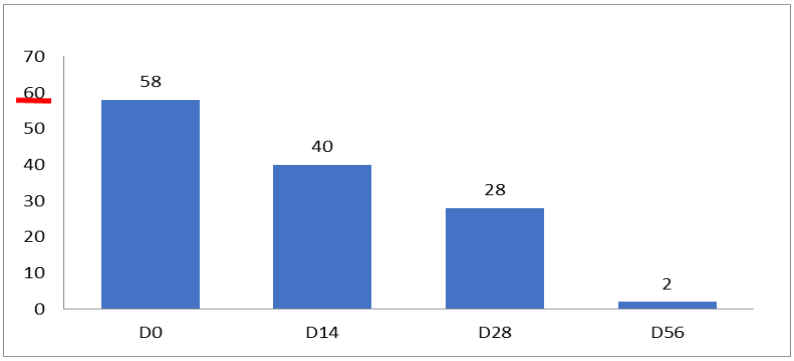


Fig. 1 – Comparative aspects of the dog Sniff at D0 (left) and at D56 (right).

Regarding the clinical score at D0 (Graph 1), it had a very close value to the maximum score of 60 (red line on the graph), reaching 56, which shows a

severely affected individual. At D14, the score reached 40, and by D28, when the second treatment was administrated, it came down to 28, meaning 48.2% of the initial value (Graph 1). By the end of the treatment, at D56, there were almost no more clinical signs of mange, the clinical resolution of the animal being around 96.5% (Graph 1).



Graph 1 – Evolution of clinical score at different time points.

Despite the fact that our study did not include a mite count, we did however resample skin scrapings from the 3 body sites at D28 and D56 and found 0 mites present, which is consistent to the other two articles regarding the efficacy of afoxolaner in treating sarcoptic mange in dog (Beugnet *et al.*, 2016; Hampel *et al.*, 2018).

In such a context, in the following, we will construct a nonlinear model which describes the dynamics of the complex system mite – canine organism, when it is constrained by external factors such as medical treatment.

Let us admit that the dynamics of the mentioned disease is described by the following differential equation

$$N = \frac{dN}{dt} = -\frac{N^2}{M} + \frac{2R}{M}N - K \tag{1}$$

where N defines the mite population, dN/dt defines the variation speed for the mite population, $(2R/M)N$ defines the saturation level of the mite population, and K defines the stabilizing level of the mite population. More precisely, the first two terms of the Eq. (1) would correspond to the interaction mite- canine organism (*i.e.* multiplication ratios of mites and the way in which the canine organism, through its immune system, reacts to the mite "attack"), while the free term would correspond to an external constraint on the mite-canine organism system, expressed through the medical treatment.

With regard to the solution of the Riccali- type Eq. (1), we must first notice that the roots of the polynomial

$$P(N) = -\frac{N^2}{M} + \frac{2R}{M}N - K \tag{2}$$

can be written as

$$N_1 = R + iM\Omega,\ N_2 = R - iM\Omega$$
$$\Omega^2 = \left(\frac{K}{M}\right) - \left(\frac{R}{M}\right)^2,\ i = \sqrt{-1} \tag{3}$$

Performing the homographic transformation

$$z = \frac{N - N_1}{N - N_2} \tag{4}$$

it results through direct calculus that z is a solution of the linear and homogenous first order equation

$$z = 2i\Omega z \tag{5}$$

which allows the solution

$$z(t) = z(0)e^{2i\Omega t} \tag{6}$$

Therefore, if the initial condition $z(0)$ is conveniently expressed, the general solution of equation (1) can be found by writing transformation (4) as

$$N = \frac{N_1 + re^{2i\Omega(t-t_r)}}{1 + re^{2i\Omega(t-t_r)}} \tag{7}$$

where r and t_r are two real constants which characterize the solution. By using relations (3) we can write this solution in real terms, as

$$z = B + A\Omega\left(\frac{2r\sin\left[2\Omega(t-t_r)\right]}{1 + r^2 + 2r\cos\left[2\Omega(t-t_r)\right]}\right) + i\frac{1-r^2}{1 + r^2 + 2r\cos\left[2\Omega(t-t_r)\right]} \tag{8}$$

which highlights a self-modulation of the pulsation type characteristic Ω, known as the Stoler transformation (Stoler, 1970; Stoler, 1971), implying a complex form for this parameter. In Fig. 2 we present this self-modulation phenomenon through Rez time dependences, for various values of r and Ω. The dependences of Rez on r and Ω (3D and contour dependences) at various scale resolutions are shown in Fig. 3.

Fig. 2a explains the evolution to chaos through period doubling of the dynamics of the complex system mite-canine organism, while Fig. 2c explains the evolution to chaos through intermittences of the dynamics of the same system. Obviously, the dependences in these figures specify only the possible criteria of evolution to chaos and not its actual presence. The evolution of antimodulation present in Fig. 2c and 2d, specifies the fact that the complex

system mite-canine organism evolves to a stability, which means, in our opinion, that the healing process has begun.

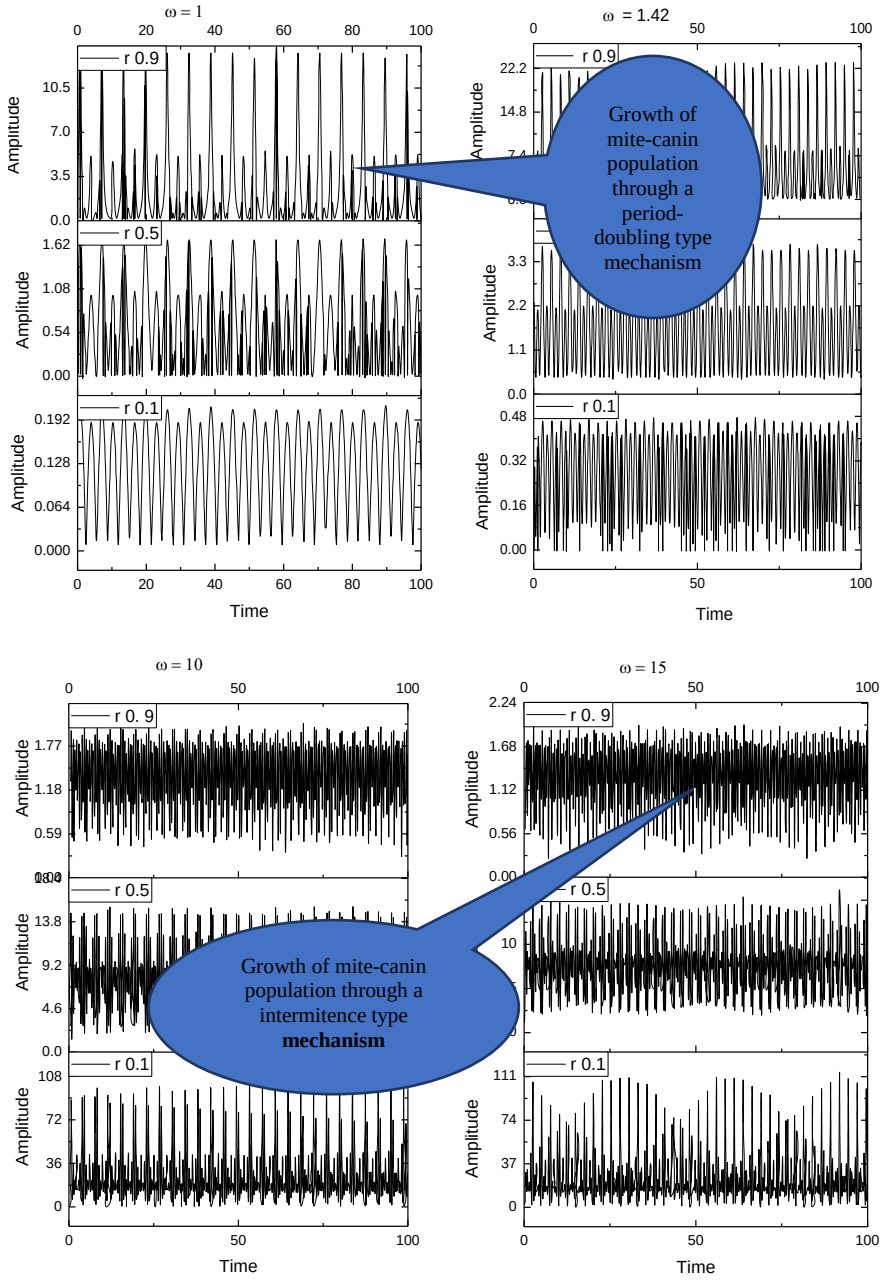


Fig. 2 – Amplitude variation with time of the Rez solution for four different values of the (pulsation-type) characteristic (1, 1.42, 10, and 15).

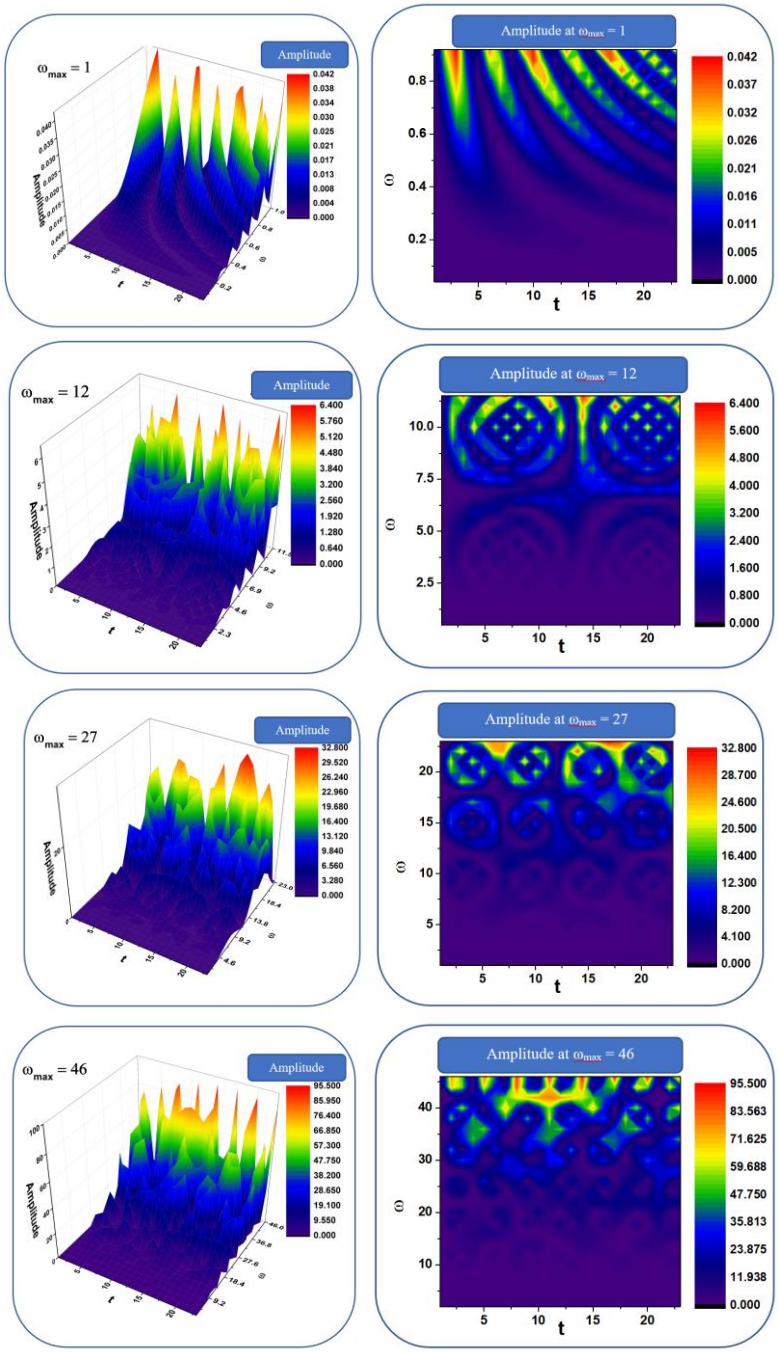


Fig. 3 – 3D and 2D representation of solution Rez at various scale resolutions given by the maximum value of the (pulsation-type) characteristic (1, 12, 27, and 46). Self-modulation of the mite-canin population growth process can be observed.

4. Conclusions

The evolution of sarcoptic mange, throughout the treatment with afoxolaner, showed a very high efficacy of this novel molecule, by reduction of the clinical score from a nearly maximum value of 56 at D0, to a value of 2, at the end of the treatment, at D56. Furthermore, there were no more mites present in skin scrapings as early as D28 and also at D56. These findings support the research from the other two studies about the efficacy of afoxolaner in treating sarcoptic mange in dogs (Beugnet *et al*., 2016; Hamepel *et al*., 2018).

The mathematical study performed regarding the relationship within the complex system mite- canine organism, showed a chaotic movement in the first part of the treatment, when mites continued to live, and marked a significant stability towards the middle to the end of the treatment, when the healing process began and the mites were eliminated.

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STUDIUL DE CAZ AL UNUI CÂINE INFECTAT CU ACARIENI *SARCOPTES SCABIEI* ŞI STUDIUL MATEMATIC AL INTERACŢIUNILOR DINTRE ACARIENI ŞI GAZDĂ

(Rezumat)

Râia sarcoptică la câini reprezintă o boală de piele cauzată de acarienii *Sarcoptes scabiei*, caracterizată de prurit intens, alopecie și formare de cruste și răni. Aceasta este o boală extrem de contagioasă.

În această lucrare prezentăm un studiu de caz al unui câine afectat sever de râia sarcoptică. Evaluarea clinică a avut loc pe tot parcursul evoluției bolii – zile (Z): Z0, Z14, Z28, Z56). Tratamentul a constat din afoxolaner, administrat în Z0 și Z28. Comparațiile scorului clinic după cele două administrări au arătat o eficacite crescută a moleculei alese.

Mai mult, s-au studiat dinamicile sistemului complex acarieni – organism canin printr-un model matematic.