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STUDY OF ACUTE TOXICITY OF DIFFERENT COMMERCIAL FORMULATIONS PEDICULICIDES

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ABSTRACT

Pediculosis is a world-wild extended ectoparasitosis with great impact on school children. There are different compounds used therapeutically against this parasitosis, but most of them have been designed to combat pests in the form of insecticides being in many cases very dangerous. The fish are used as models to determine the acute toxicity through the measuring the mortality of various species. In this work we evaluated the acute toxicity of ten formulations of pediculicides formulated with different actives principles by using fish (*Poecilia reticulate*). The results showed that pediculicides formulated with natural products are less toxic compared with those formulated with synthetic products. The toxicity varies and depends mainly on the type and concentration of active ingredient. Our results indicate that it is not justified to use pediculicides formulated with lindane because it is significantly more toxic than any of the pediculicides available.

Key Words:- Pediculicides, Acute toxicity, Fish.

INTRODUCTION

Pediculus capitis (*Anoplura; Pediculida*) is the responsible agent of pediculosis a world-wild extended ectoparasitosis with great impact on school children (Araújo *et al*., 2000). There are different compounds used therapeutically against this parasitosis which possess different active agents as well as different pharmaceutical formulations. In South America the most used agents are: piretrine (permetrine, aletrine detametrine or decametrine and d-phenotrine or sumithrine), organophosphorate compounds (malathion), organochlorated compounds (lindane) essential oils and acetic acid among others. The only agents approved by the FDA for treatment of pediculosis are lindane and malathion (McMichael *et al*., 2008), both classified as category B (Kimberly *et al*., 2003).

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Most of them have been designed to combat pests in the form of insecticides, displayed different degrees of toxic effects on the host, being in many cases very dangerous.

In the last years it has been several attempts trying to obtain new methods to detect and evaluate the acute toxicity. The fish are used as models to determine the acute toxicity through the measuring the mortality of various species (Ballesteros *et al.*, 2009 and Lushchak *et al*., 2009). Our research group has previously used fish to assess the potential toxicity of different novel drugs of natural and/or synthetic source (Bisogno *et al*., 2007 and Garibotto *et al*., 2010).

The principal goal of this communications is to analyze the acute toxicity of ten formulations of pediculicides formulated with different actives principles. In our study we evaluated the acute toxicity by using fish (*Poecilia reticulate*), species which has been previously used in acute toxicity test (Slooff *et al*, 1983).

MATERIAL AND METHODS

Formulations of pediculicides

The pediculicides formulations evaluated were obtained in 2011 in local shops and studies were carried out in 2012. The evaluated formulations are presented in Table 1.

Acute toxicity test

The toxic effect of formulations was evaluated starting from a concentration of 01% of the commercial formulation by using a toxicity test on *Poecilia reticulata* fish. The static technique recommended by the US Fish and wildlife Service Columbia National Fisheries Research Laboratory (Johnson *et al.*, 2008) was modified in order to use lower amounts of tested compounds (Mascotti *et al*.,2008). The fish were born and grown in our laboratory until they reached a size of 0.7–1 cm (15 days old). In the toxicity test, 10 specimens were exposed to each of the concentration tested per drug in 2 L wide-mouthed jars containing the test solutions. The test began upon initial exposure to the solutions and continued for 96 hs. The number of dead organisms in each test chamber was recorded and the dead organisms were removed every 24 h; general observations on the conditions of tested organisms were also recorded at that time; however the percentage of mortality was recorded at 96 hs. Each experience was performed two times with three replicates each. It was determined the minimum concentration of formulated which produced 100% mortality (MC100% M) and the maximum concentration that did not cause mortality (MC0% M).

Statistical Analysis

For acute toxicity results of the chi-square method is applied to analyze and compare the frequencies between mortality rates from acute toxicity tables of different solutions to fish. For comparisons between the minimum doses that produced 100% mortality and maximum doses that produce 0% mortality Student test nonparametric Mann-Whitney was applied.

RESULTS AND DISCUSSION

Different concentrations of the commercial formulations were evaluated starting from 0.1% of concentration (volume of commercial formulation/volume of water) and then by performing systematic dilutions until obtain the minimal concentration which no displays mortality in the experimental model used. The results obtained are summarized in table 2.

The less toxic Pediculicides evaluated against the experimental model used, were C and H which do not produce mortality concentration values up to 1% of sample. The active principles of these pediculicides are natural compounds, mainly essential oils so its use would be advantageous if we also consider that the complexity of the active ingredients might prevent the rapid development of resistance (Mumcuoglu *et al.*, 1991).

The rest displayed a variable toxicity, with the G sample, whose active ingredient is Permethrin giving a high toxicity. Pediculicide E, whose active ingredient is Permethrin, shows less toxicity than the previous one, but it should be noted that it is one lotion. The toxicity of the pediculicide J formulated with lindane, is significantly superior to all, even ten times more than the pediculicide G; this data this data as existing reports the intrinsic toxicity of the compound (Friedman *et al*., 1987 and Pollack *et al*., 1999) justifies the prohibition in some countries to use this active substance (ANMAT, Comunicados, 2011 and Chile, Instituto de Salud Pública, 2009).

Table 1. Pediculicides evaluated; concentration of active principle and pharmaceutical form

Sample	Principio/s Activo/s	Concentration	Pharmaceutical form
A	d-phenothrin	3 mg/ml	lotion
B	deltamethrin piperonyl butoxide	0.22 mg/ml 1.10 mg/ml	lotion
C	citrus essential oils	No reported	lotion
D	garlic extract	No reported	cream rinse
E	permethrin	10 mg/ml	cream rinse
F	benzyl alcohol N, N diethyl toluamide acetylamino butyl ethyl propionate	1.5 % 3 % 1.5 %	cream rinse
G	permethrin	10 mg/ml	lotion
H	eucalyptus essential oil lavanda essential oil chlorophyll copper complex	2.0 % 0.5 % 0.04 %	lotion

I	copper oleate	10 mg/ml	shampo
J	lindane	1 %	shampo

Table 2. Minimum concentration which produced 100% mortality (MC100% M) and the maximum concentration that did not cause mortality (MC0% M) of ten formulations evaluated

Sample	MC 100% M	MC 0% M	Sample	MC 100% M	MC 0% M
A	0.1 %	0.01 %	**F**	0.1 %	0.01 %
B	0.001 %	0.0001 %	**G**	0.0001 %	0.00001 %
C	Nd	≥ 1 %	**H**	Nd	≥ 1 %
D	0.1 %	0.01 %	**I**	0.001 %	0.0001 %
E	0.001 %	0.0001 %	**J**	0.00005 %	0.000001 %

Nd: not determinated

CONCLUSIONS

In the experimental model used here, pediculicides formulated with natural products are less toxic with respect to those formulated with synthetic products. Among natural products, the essential oils are those having least toxicity. The toxicity of pediculicides varies and depends mainly on the type and concentration of the active ingredient and in a lesser degree of importance, of the type of pharmaceutical form. Our results are an additional support in order to not utilize pediculicides formulated with lindane because they are significantly more toxic than any of the pediculicides available.

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CONFLICT OF INTEREST: None

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