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Substance Harmful to Parasitic

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Abstract- Introduction: The parasites have mechanisms that can help and help escape the host's immune actions, infiltrating and infecting for a long time, and that when discovered the disease is already in the critical period. It is possible to observe in the scientific environment the use of different methods that contribute to the diagnosis of diseases like this one. Among them, bio informatics emerges, offering computational tools related to biological problems, including applications that promote human health, and contributing to the planning of new drugs. Objective: To identify virtually noxious substances to the parasite and its behavior in vertebrate beings, through the interaction of data, with the aid of computational tools. Methodology: The study presents a transverse character and quantitative analysis. The population of the referred study will be composed of research data that relate possible harmful substances to the parasite T.cruzi. Next, the search for interactions will be performed using programs like String, Stitch and Cytoscape, from the database with all available information. Results: The analysis of the Stitch program provided five substances that had interactions with the parasite, but only two were propitious to be harmful to T.cruzi, due to the relationship between the parasite proteins and Homo Sapiens in Cytoscape, which did not present any results. The interactions achieved were only between the same species. Conclusion: However, the present study opens the door to more research on in vivo behavior in humans for the possibility and feasibility of formulating new drugs, contributing to the health of patients with Chagas disease.
Keyword: Bioinformatics. Chagas disease. Protein interactions.

I. INTRODUCTION

The parasites have mechanisms that can aid and help escape the host's immune actions, infiltrating and infecting for a long time, and when discovered, the disease is already in the critical period [10]. Trypanosoma cruzi, the etiological agent of Chagas' disease, has several forms of defense, depending on its habitat. In the vector the parasite presents in the forms of amastigotes, epimastigotes and metacyclic trypomastigotes. In the human host, it is shown as amastigotes, trypomastigotes of broad and thin forms, and are rarely found in its epimastigote form since they cannot develop and multiply in the human host [11]. Chagas disease has two stages. There is an acute phase that occurs in the first days of parasite infection, which may be symptomatic or asymptomatic. According to [11], this phase is characterized by local manifestations, when T. Cruzi enters the conjunctiva (Romaña sign) or on the skin (chagoma of inoculation). In the chronic symptomatic phase, certain numbers of chagasic patients remain asymptomatic for several years, presenting symptoms with the cardiocirculatory system, digestive system, or both, which will cause chronic chagasic cardiopathy, mega esophagus and mega colon, [12]. However, the chronic phase does not present alternatives for treatment [6].

T.cruzi during the acute phase replicates extensively, releasing immunomodulatory molecules that hinders the response mediated by the defense cells, allowing the parasite to spread through the host. In the chronic phase, avoidance most likely depends on the sequestration of the TGF-β receptor (Beta Growth Transforming Factor) of the host that helps in tissue regeneration. Thus, it causes the replication rate and impairment to persist in the chronic phase of infection [7]. This parasite also has the means to manipulate cellular signaling processes, crossing barriers such as the host's immune system and obtaining conditions for its development [1].

It is possible to observe in the scientific environment the use of different methods that contribute to the diagnosis of diseases such as, for example, sores. Bioinformatics offers computational tools related to biological problems, including applications that favor human health, such as for the planning of new drugs [8]. This approach refers mainly to the elucidation and studies of parasite proteins that have been studied and exploited for therapeutic purposes. The enzyme cruzaína was investigated by [4], in which it objectified in its work to identify new inhibitors of this enzyme that could be candidates for drugs for the disease of sores. In this work a virtual screening based on the receptor structure (SBVS) was carried out, which allowed the selection of new candidates for target protein ligands in large databases of compounds. With this methodology, the author identified 18 compounds that were included for trials, six of which presented inhibitory activity.

The evidence is a disease of sores, with the possibility of occurrence of powerful drugs as a disease of sores, with the possibility of being eliminated [13]. The strengthening of new research involving the destruction of the parasite and the treatment of diseases in science and technology [6].

Considering the above, the objective of the present study was to identify virtually harmful substances to the parasite and its behavior in vertebrate beings, through the interaction of data, with the help of computational tools.

II. MATERIAL AND METHODS

The study presented transverse character and quantitative analysis. The population of the present study was composed by the content related to the etiologic agent of Chagas' disease, present in the various databases available on the Internet. The sample consisted of researches that included the possible harmful substances to T. cruzi parasite. In order to reproduce this interaction, the software STRING (version 10.5), STITCH (version 5.0) and CYTOSCAPE (version 3.5.1) were used, where they have a database with all the available information.

The harmful substances and the T.cruzi genes were searched in large-scale gene databases. To determine the major set of genes, searches were performed on the following databases: PubMed, Gene-Bank, Gene Atlas and GeneCards. Next, the T. cruzi genes that were selected for the search for interactions with a species of Homosapiens were transferred to STRING. Subsequently, no STITCH software was searched for interactions between substances harmful to the parasite. The STRING and STITCH software were used to mark each interaction to construct the map of interaction between the genes identified.

Thus, the interactions obtained were joined by CYTOSCAPE to visualize complex networks and integrate them with any type of attribute data.

The obtained data were analyzed and arranged in interaction networks to better visualize the results.

III. RESULTS AND DISCUSSION

Initially, the analysis of the present study was based on a list containing 20 harmful substances, all being heavy metals. Such choice was based on chemical interaction with the biological system in various ways, and toxicity on various types of living beings, in this case the parasite [18]. In the STRING relations between the T.cruzi genes in Homosapiens did not present any results. In part, STITCH, we examined the relationship between the 20 substances and their possible interactions with proteins involved in Trypanosoma cruzi and Homosapiens.

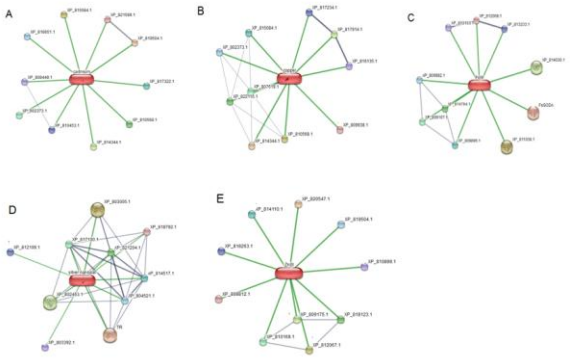
The preliminary analysis showed five substances that had interactions with the parasite, but only two were propitious to be harmful to T.cruzi (Fig.1) (Tab.1).

Table.1 Proteins of the interaction between substances harmful to T. cruzi.

N°	A CADMIUM	B COPPER	C IRON	D SILVER	E ZINC
1	XP_815084.1	XP_817234.1	XP_810103.1	XP_803005.1	XP_820547.1
2	XP_821599.1	XP_817914.1	XP_812008.1	XP_818792.1	XP_819504.1
3	XP_819504.1	XP_816135.1	XP_813233.1	XP_821204.1	XP_810899.1
4	XP_817322.1	XP_809938.1	XP_814030.1	XP_814517.1	XP_818123.1
5	XP_810568.1	XP_810568.1	FeSODA	XP_804521.1	XP_812067.1
6	XP_814344.1	XP_814344.1	XP_811038.1	TR	XP_809175.1
7	XP_810453.1	XP_807619.1	XP_809896.1	XP_803392.1	XP_810169.1
8	XP_802373.1	XP_822115.1	XP_814764.1	XP_802453.1	XP_808812.1
9	XP_808449.1	XP_802373.1	XP_809107.1	XP_812199.1	XP_818263.1
10	XP_818651.1	XP_815084.1	XP_809882.1	XP_817100.1	XP_814110.1

Source: Research data, 2018.

Figure 1-The figure shows the interaction map between the substances harmful to T.cruzi.



Source: Research data, 2018.

Among them, iron (Fig. 1C) in which one of the papers reports on the effects of prolonged treatment with iron chelator on the development of infection in rats inoculated with Trypanosoma cruzi. Infected and treated rats were found to have lower levels of Parasitaemia and reduced mortality rate compared to infected and untreated animals. If the hypothesis that iron is important for the proliferation of T. cruzi is valid, then the removal of heavy metal through the use of a chelator could moderate the proliferation of the parasite and thus reduce its blood levels [14].

Based on the STITCH in Figure 1C, the interaction protein 2 has the function of helping in the synthesis of DNA and in interactions 5, 6 and 7 proteins have as their function to destroy radicals that are produced in the parasite itself and that are toxic to it, decrease or absence of iron may lead to the destruction of the parasite.

As for zinc (Fig. 1E), it was observed the possibility that, when used as a treatment in mice, the T. cruzi reduction by mono nuclear phagocytes. A short incubation of ZnCl2, but not other metals in mono nuclear phagocyte-deficient mice, completely restored the ability to produce larger amounts of H2O2, reducing T. cruzi in the body due to a heavy metal function in the elimination process or in the production of some other important agent [15].

The other three substances copper, cadmium and silver in their interactions were not found proteins that are important to the parasite and that in their lack or accumulation can cause death to the same.

In relation to the interaction with Homosapiens, only those whose substances had a positive result for T. cruzi (Fig. 2) (Tab.2) were made. Between the two iron and zinc substances that are harmful to the parasite, zinc (Fig. 2E) shows the interaction with protein 3 that has as a probable auxiliary function in the destruction of radicals manufactured in humans and which are toxic to the same.

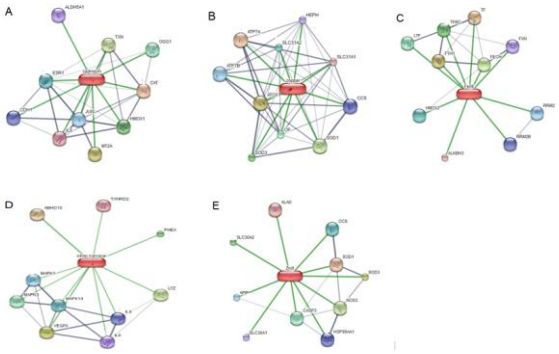
Table 2 Proteins of the interaction between harmful substances recognized by T.cruzi to homosapiens.

N°	A CADMIUM	B COPPER	C IRON	D SILVER	E ZINC
1	ALDH5A1	HEPH	TF	TXNRD2	ALAD
2	TXN	SLC31A1	FXN	PHEX	CCS
3	OGG1	CCS	FECH	LYZ	SOD1
4	CAT	SOD1	RRM2	IL8	SOD3
5	HMOX1	SOD3	RRM2B	IL6	NOS3
6	MT2A	ATOX1	ALKBH3	VEGFA	HSP90AA1
7	JUN	ATP7B	HMOX2	MAPK14	CASP3
8	IL6	ATP7A	FTH1	MAPK3	SLC30A1
9	CDH1	CP	LTF	MAPK1	APIP

10	ESR1	SLC31A2	TFRC	ABHD10	SLC30A2

Source: Research data, 2018.

Figure 2- The figure shows the interaction map between the harmful substances recognized by T.cruzi to homosapiens.



Source: Research data, 2018.

The interactions between harmful substances recognized for the parasite and the gene recognized in Homosapiens by Cytoscape did not present any results (Fig. 3). The interactions reached were only between the same species, it being understood that the species only united because of the heavy metals.

Some of these metals can be dangerous if they are inserted directly into humans, and can act as catalytic centers in oxidation, producing bio molecular modifications in proteins or DNA [2], however, there are some alternatives in the treatment of some infections, where metals are used. The inclusion of silver in nanoparticles in treatment, also referred to as colloidal silver, may be beneficial as it acts against a broad range of microorganisms such as bacteria, fungi and viruses, cells infected with HIV-1. This effect may possibly arise from the production of proteins that would act as chelates by complexing the silver, thus reducing its toxicity [16].

Some studies report the advance of platinum-based compounds in the treatment of cancer, however, some researchers have directed their attention to the development of new drugs through metals, such as gold used in the treatment of rheumatoid arthritis [17].

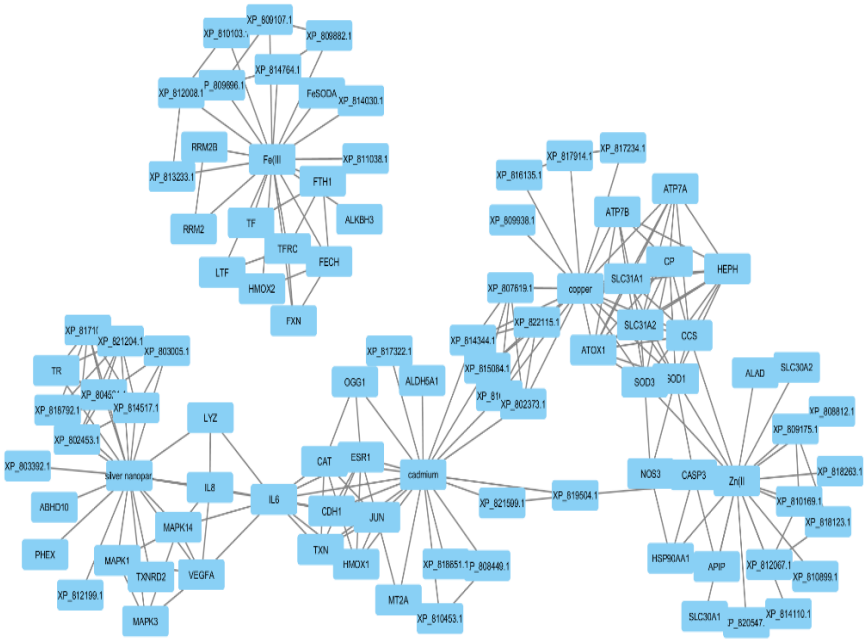


Figure 3- Interaction between T. cruzi genes with Homosapiens and heavy metals, using Cytoscape.

IV. CONCLUSION

There are substances that are harmful to T. cruzi and can also be found in humans, and that the removal or incorporation of them may influence the reduction of the parasite in the organism. However, the present study opens the door to more research on in vivo behavior in humans for the feasibility and feasibility of formulating new drugs, contributing to the health of patients with diseases of sores.

V. REFERENCE

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