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# Neuroprotective Potential of a Polyherbal Formulation in Enhancing Mental Clarity and Emotional Stability

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ABSTRACT:
Chagas is one of the most common illnesses in Latin America. Chagas and Trypanosomacruzi are treated with benznidazole and nifurtimoxis, but these treatments are unsuccessful in the chronic phase of epimastigote and El Salvador. Thus, there is an urgent need for the creation of new medications, particularly for the chronic stage of the illness, according to the author. We examined 114 plant species from the Salvadoran flora using the in-vitro anti-Marvin J. Núñez trypanosome assay, and 34 active plants against the stepimastigote of Trypanosomacruzi Research Scholar were found
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**INTRODUCTION**

Trypanosoma cruziprotozoan is the causative agent of Chagas disease, which affects 6–7 million individuals in Latin America and results in around 50,000 fatalities annually. However, between 65 and 100 million individuals are infected. danger 1. Important epidemiological data from a research on Chagas disease in El Salvador from 2018 to 2020 included a 2.3% seropositivity rate for juvenile Chagas in Sonsonate and a 34.4% infection incidence among triatomines, which are disease vectors. A maternal surveillance study conducted in 2022 revealed that 6% of pregnant women tested positive for T. cruzi2. 52 acute and 894 chronic suspected Chagas cases were recorded by the Ministry of Public Health during that year. 3. Natural products originating from plants are crucial for medication development and discovery because they provide a wealth of bioactive compounds with a variety of characteristics. Actually, medicinal plants are the source of 25% of presently available medications. This is particularly crucial in areas where trypanosomiases are common. El Salvador and other nations with a wealth of medicinal plant resources are of specific importance. In vitro tests have shown that several of these plants and their components are effective against T. cruzi 5,6. Here, we provide the in vitro anti-T. cruzi epimastigotes activity of 114 plant species from 14 botanical groups. Interestingly, antitrypanosomal activity was present in about 30% of the species that were tested.

## RESOURCES AND METHODS:

Choosing Plants: The species were chosen in light of the findings of a previous study5, which showed that several families and botanical genera found

in the Salvadoran flora showed promise. Jenny Elizabeth Menjívar Cruz from the Museum of Natural History in El Salvador and Gabriel Cerén from the Escuela de Biología, Universidad de El Salvador, identified 114 plant species that were gathered in various parts of El Salvador between 2019 and 2022. For every species, a voucher specimen has been placed at the MHES Herbarium. Table 1.
Plant Extract Preparation: Following 48 to 72 hours of drying at 40 °C in an air-circulating oven (BIOBASE, China, model BOV-V225F), the plants indicated in Table 1 were ground to a particle size of less than 2 mm (Bel-Art products, USA, model micro-mill). Using a magnetic stirrer and an ultrasonic bath (VWR, USA, model 97,043-988, operating frequency 35 kHz), 20 grams of each sample were extracted over 90 minutes at 25 °C. To produce the crude MeOH extracts, each extract was concentrated at 40°C under decreased pressure (model RE801, Yamato Scientific Co., Ltd., Japan).

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**TABLE 1: ANTITRYPANOSOMAL ACTIVITY OF SALVADORAN SPECIES AGAINST EPIMASTIGOTE STAGE OF T*RYPANOSOMA CRUZI***

| Family/Scientificname | Plantpartused | Voucher/Place | Viability(%) | |
|---|---|---|---|---|
| | | | 100 µg/mL | 10 µg/mL |
| Acanthaceae | Aerialparts | | | |
| *Aphelandrascabra*(Vahl)Sm. | | GC-4819/1 | 48.19±3.78 | 72.46±0.93 |
| *Ruelliainundata*Kunth | Aerialparts | GC-4816/1 | 49.60±2.40 | 78.62±5.89 |
| Achatocarpaceae | Aerialparts | | | |
| *Achatocarpusnigricans*Triana | | GC-4811/1 | 62.67±3.98 | 72.28±7.47 |
| Anacardiaceae | Leaves | | | |
| *Schinusterebinthifolia*Raddi | | GC-5657/2 | 75.75±1.26 | 77.42±8.12 |
| Annonaceae | Leaves | GC-5233/3 | 46.07±2.49 | 75.09±1.69 |
| *Annonacherimola*Mill. | Stembark | GC-5233/3 | 69.50±10.22 | 93.30±5.02 |
| *Annonaholosericea*Saff. | Stembark | GC-5326/4 | 8.82±0.52 | 89.45±10.25 |
| *Annonareticulata*L. | Stembark | GC-519/5 | 88.91±1.27 | 100.29±8.56 |
| *Sapranthusmicrocarpus*(Donn.Sm.)R.E.Fr. | Leaves | GC-5029/6 | 58.43±2.45 | 81.88±8.33 |
| | Aerialparts | GC-5272/8 | 57.31±11.39 | 85.86±10.29 |
| *Sapranthusviolaceus*(Dunal)Saff. | Leaves | GC-5148/4 | 68.09±11.51 | 80.89±2.61 |
| | Stembark | GC-5148/4 | 55.70±10.14 | 80.38±7.85 |
| Apocynaceae | | | | |
| *Alstonialongifolia*(A.DC.)Pichon | Aerialparts | GC-4823/1 | 34.75±0.72 | 78.07±1.45 |
| *Echitesyucatanensis*Millsp.exStandl. | Leaves | GC-4888/7 | 60.36±5.94 | 76.61±6.80 |
| *Ruehssiaveronicae*(W.D.Stevens)L.O.Alvarado | Aerialparts | GC-5341/4 | 78.11±8.11 | 91.14±5.27 |
| Aristolochiaceae | | | | |
| *Aristolochiaanguicida*Jacq. | Aerialparts | JM-5121/9 | 50.90±9.72 | 96.05±4.98 |
| *Aristolochiagrandiflora*Sw. | Aerialparts | GC-5190/5 | 67.50±4.35 | 82.78±4.49 |
| *Aristolochiamaxima*Jacq. | Aerialparts | JM-5122/9 | 80.53±8.30 | 104.13±4.89 |
| *Aristolochiastevensii*Barringer | Aerialparts | JM-5128/10 | 81.88±8.74 | 106.35±1.42 |
| Asteraceae | | | | |
| *Ageratumcorymbosum*Zuccagni | Aerialparts | JM-4634/11 | 47.46±5.32 | 94.02±1.84 |
| *Caleaurticifolia*DC. | Leaves | GC-5656/2 | 2.17±0.65 | 56.17±8.3 |
| *Chromolaenaodorata*(L.)R.M.King&H.Rob. | Aerialparts | JM-5216/12 | 59.96±13.36 | 72.09±1.67 |
| *Eremosisleiocarpa*(DC.)Gleason | Aerialparts | GC-5150/4 | 8.82±1.71 | 75.39±6.20 |
| *Fleischmanniahymenophylla*(Klatt)R.M.King& H.Rob. | Aerialparts | JM-4647/10 | 80.03±3.16 | 99.91±1.61 |
| *Fleischmanniapratensis*(Klatt)R.M.King&H.Rob. | Aerialparts | JM-4646/10 | 93.79±0.90 | 97.34±6.24 |
| *Fleischmanniopsisleucocephala*(Benth.)R.M.King &H.Rob | Aerialparts | GC-4885/7 | 50.83±5.79 | 75.30±5.03 |
| *Lepidaploacanescens*(Kunth)H.Rob. | Aerialparts | JM-5217/12 | 65.17±3.50 | 75.13±3.85 |
| *Perymeniumnicaraguense*S.F.Blake | Leaves | JM-5149/12 | 73.37±4.22 | 101.94±2.04 |
| *Salmeascandens*DC. | Aerialparts | GC-4857/13 | 45.67±1.82 | 80.78±9.89 |
| *Schistocarphahondurensis*Standl.&L.O.Williams | Aerialparts | GC-4856/13 | 50.79±8.75 | 73.50±7.31 |
| *Tagetesfilifolia*Lag. | Wholeplant | GC-4710/12 | 92.13±8.61 | 102.61±10.23 |
| *Tagetestenuifolia*Cav. | Aerialparts | JM-5205/11 | 67.95±11.21 | 92.13±3.59 |
| *Verbesinaturbacensis*Kunth | Aerialparts | JM-5218/12 | 67.96±8.98 | 92.33±4.76 |
| *Vernonanthurapatens*(Kunth)H.Rob. | Aerialparts | GC-5152/4 | 74.78±3.26 | 85.56±5.95 |
| Bixaceae | | | | |
| *Cochlospermumvitifolium*(Willd.)Spreng. | Stembark | GC-5273/8 | 74.95±7.44 | 88.32±8.55 |
| Boraginaceae | | | | |
| *Cordiapanamensis*L.Riley | Leaves | GC-5030/6 | 58.58±9.90 | 93.33±8.42 |
| | Stembark | GC-5325/4 | 77.15±7.41 | 90.10±4.64 |
| Burseraceae | | | | |
| *Burserabipinnata*Engl. | Stembark | GC-5317/4 | 59.05±12.55 | 108.08±2.60 |
| Campanulaceae | | | | |
| *Lobelialaxiflora*Kunth | Aerialparts | GC-5134/4 | 60.25±8.01 | 87.09±1.52 |
| Capparaceae | | | | |
| *Cratevatapia*L. | Leaves | GC-4830/1 | 50.37±1.01 | 80.86±6.35 |
| Convolvulaceae | | | | |
| *Ipomoeaalba*L. | Aerialparts | GC-5031/6 | 82.26±7.03 | 89.13±3.41 |

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|---|---|---|---|---|
| *Ipomeawolcottiana*Rose | Leaves | GC-5274/8 | 49.10±2.83 | 84.38±12.88 |
| | Stembark | GC-5274/8 | 92.66±7.33 | 98.17±6.36 |
| *Ipomoeaaurantiaca*L.O.Williams | Aerialparts | GC-5309/4 | 76.09±7.08 | 84.59±1.48 |
| Ericaceae | | | | |
| *Gaultheriaerecta*Vent. | Leaves | JM-5201/11 | 75.60±3.73 | 97.47±5.91 |
| Erythroxilaceae | | | | |
| *Erythroxylummexicanum*Kunth | Leaves | GC-4976/8 | 55.09±6.10 | 85.70±4.88 |
| Euphorbiaceae | | | | |
| *Acalyphafirmula*Müll.Arg | Aerialparts | JM-5148/12 | 59.78±3.07 | 87.03±1.68 |
| *Crotonpseudoniveus*Lundell | Leaves | GC-4979/8 | 77.37±9.00 | 98.49±5.44 |
| *Crotonrepens*Schltdl. | Aerialparts | GC-4682/12 | 69.99±3.83 | 96.90±4.09 |
| *Omphaleaoleifera*Hemsl | Stembark | GC-5281/8 | 77.42±0.96 | 93.00±2.28 |
| Fabaceae | | | | |
| *Crotalariasagittalis*L. | Aerialparts | GC-4984/6 | 73.00±7.34 | 101.95±1.73 |
| *Crotalariavitellina*KerGawl. | Aerialparts | GC-4995/6 | 61.06±2.82 | 86.28±13.13 |
| *Desmodiumnicaraguense*Oerst. | Aerialparts | GC-4815/1 | 58.61±14.75 | 84.64±12.44 |
| *Erythrinalanceolata*Standl. | Aerialparts | GC-5328/4 | 76.60±1.56 | 91.27±3.44 |
| *Leptolobiumpanamense*(Benth.)Sch.Rodr.& A.M.G.Azevedo | Leaves | GC-5158/4 | 67.73±10.85 | 82.17±11.92 |
| *Lonchocarpusphaseolifolius*Benth. | Stembark | GC-5278/8 | 87.45±5.30 | 89.32±12.09 |
| *Machaeriumbiovulatum*Micheli | Leaves | GC-4968/8 | 78.03±4.12 | 84.02±8.41 |
| *Machaeriumkegelii*Meisn. | Leaves | GC-4905/7 | 67.43±4.18 | 81.44±0.97 |
| *Machaeriumpittieri*J.F.Macbr. | Aerialparts | GC-4782/4 | 48.09±5.86 | 72.35±4.10 |
| | Leaves | GC-4899/7 | 71.09±5.33 | 88.16±8.12 |
| *Mimosadiplotricha*C.Wright | Aerialparts | JM-5146/12 | 76.21±4.36 | 98.85±9.79 |
| *Mimosapudica*L. | Aerialparts | JM-5136/14 | 65.19±2.55 | 88.52±3.31 |
| *Pachyrhizuserosus*(L.)Urb. | Aerialparts | GC-4678/12 | 78.25±12.78 | 91.01±4.89 |
| *Poiretiapunctata*(Willd.)Desv. | Aerialparts | GC-5021/6 | 67.86±2.89 | 81.85±2.21 |
| *Rhynchosiaphaseoloides*(Sw.)DC. | Leaves | GC-5199/15 | 76.34±12.96 | 100.73±6.01 |
| Fagaceae*Quercusskinneri*Benth. | Leaves | GC-5261/16 | 58.75±11.19 | 85.17±4.92 |
| Gesneriaceae | | | | |
| *Drymoniaserrulata*Mart. | Aerialparts | GC-5024/6 | 75.03±8.04 | 87.40±2.57 |
| Lamiaceae | | | | |
| *Hyptiscapitata*Jacq. | Aerialparts | GC-4788/4 | 61.47±7.42 | 79.34±12.96 |
| *Salviaurica*Epling | Aerialparts | GC-4676/12 | 64.82±11.28 | 81.70±2.33 |
| Lauraceae | | | | |
| *Damburneyamartinicensis*(Mez)Trofimov | Branch | JM-5125/10 | 66.33±11.68 | 92.57±2.86 |
| *Ocoteasinuata*(Mez)Rohwer | Leaves | JM-5131/10 | 59.95±11.78 | 108.74±5.77 |
| Malvaceae | | | | |
| *Helicteresguazumifolia*Kunth | Aerialparts | GC-5020/6 | 57.89±7.49 | 80.72±10.90 |
| Meliaceae | | | | |
| *Trichiliamartiana*C.DC. | Fruit | GC-4892/7 | 75.33±8.96 | 85.04±2.67 |
| *Trichiliatrifolia*L. | Leaves | JM-5116/9 | 40.05±13.56 | 85.14±12.67 |
| Myricaceae | | | | |
| *Myricacerifera*L. | Leaves | JM-5197/11 | 61.65±13.19 | 78.23±12.09 |
| Myrtaceae | | | | |
| *Eugeniacacuminum*Standl.&Steyerm. | Leaves | GC-4789/4 | 28.06±12.49 | 82.25±2.39 |
| Onagraceae | | J | | |
| *Fuchsiamicrophylla*subsp.*chiapensis*(Brandegee) | Leaves | M-5199/11 | 58.63±11.95 | 91.89±3.12 |
| P.E.Berry & Breedlove | Branch | JM-5199/11 | 67.40±9.00 | 100.71±7.36 |
| Phytolaccaeae | | | | |
| *Phytolaccarugosa*A.Braun&C.D.Bouché | Aerialparts | GC-4859/13 | 62.94±3.22 | 87.11±8.12 |
| Piperaceae | | | | |
| *Peperomiabernouillii*C.DC. | Wholeplant | GC-5182/5 | 39.15±6.72 | 74.95±9.20 |
| *Peperomiagalioides*Kunth | Aerialparts | GC-4842/13 | 49.09±6.68 | 82.89±9.89 |
| *Peperomialanceolatopeltata*C.DC. | Wholeplant | JM-5137/14 | 46.04±10.81 | 85.92±9.93 |
| *Peperomialancifolia*Hook. | Wholeplant | GC-5186/5 | 42.79±5.00 | 73.61±1.93 |
| *Peperomialignescens*C.DC | Wholeplant | GC-4920/17 | 48.86±0.31 | 90.76±3.46 |
| *Peperomiapseudoalpina*Trel. | Wholeplant | GC-5105/4 | 1.25±0.35 | 68.18±7.78 |
| *Peperomiasanfelipensis*C.DC.exDonn.Sm. | Aerialparts | GC-4845/13 | 44.68±4.68 | 88.68±0.86 |

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|---|---|---|---|---|
| *Piperaduncum*L. | Aerialparts | GC-4784/4 | 30.88±12.50 | 76.03±4.31 |
| *Piperamalago*L | Leaves | GC-4814/1 | 3.22±1.20 | 66.24±8.73 |
| *Piperglabrescens*C.DC. | Aerialparts | GC-4790/4 | 37.56±7.35 | 72.56±3.79 |
| *Pipermartensianum*C.DC. | Aerialparts | GC-4785/4 | 1.62±0.50 | 70.22±7.36 |
| *Pipermarginatum*Jacq. | Aerialparts | GC-5184/5 | 57.08±3.78 | 76.67±5.04 |
| *Pipertuberculatum*Jacq. | Leaves | GC-4963/8 | 17.79±11.17 | 83.46±5.06 |
| *Piperyucatanense*C.DC. | Aerialparts | GC-4962/8 | 25.48±5.57 | 71.97±11.69 |
| Podocarpaceae | | | | |
| *Podocarpusoleifolius*D.Don | Leaves | JM-5129/10 | 48.27±11.31 | 95.27±15.35 |
| Polygalaceae | | | | |
| *Asemeiaviolacea*(Aubl.)J.F.B.Pastore&J.R.Abbott | Aerialparts | GC-4680/12 | 62.35±8.69 | 98.13±11.22 |
| *Polygalapaniculata*L. | Aerialparts | GC-5654/12 | 51.42±12.67 | 88.83±9.17 |
| Proteaceae | | | | |
| *RoupalaMontana*Aubl. | Leaves | JM-5203/11 | 81.57±5.57 | 118.36±13.42 |
| Rhamnaceae | | | | |
| *Karwinskiacalderonii*Standl. | Leaves | GC-4778/4 | 60.30±3.65 | 81.73±5.26 |
| Rubiaceae | | | | |
| *Arachnothryxlaniflora*(Benth.)Planch. | Aerialparts | GC-4853/13 | 54.68±7.42 | 72.94±4.02 |
| *Calycophyllumcandidissimum*(Vahl)DC. | Stembark | GC-5280/8 | 79.67±3.38 | 71.89±2.69 |
| *Coccocypselumhirsutum*Bartl.exDC. | Fruit | GC-5655/12 | 110.89±3.81 | 104.42±6.63 |
| *Donnellyanthusdeamii*(Donn.Sm.)Borhidi | Leaves | GC-5028/6 | 71.19±13.24 | 77.01±7.47 |
| *Geophilarepens*(L.)I.M.Johnst. | Wholeplant | GC-4966/8 | 66.77±6.10 | 86.19±9.58 |
| *Palicoureapadifolia*(Willd.exSchult.)C.M.Taylor &Lorence | Root | GC-5259/13 | 95.81±2.89 | 102.32±4.73 |
| *Palicoureapubescens*(Sw.)Borhidi | Aerialparts | GC-5225/15 | 64.33±11.29 | 98.69±2.41 |
| *Randiamonantha*Benth. | Leaves | GC-4828/1 | 18.79±7.37 | 77.73±11.37 |
| *Rovaeanthusstrigosus*(Benth.)Borhidi | Aerialparts | JM-5200/11 | 90.55±2.05 | 101.99±3.18 |
| *Solenandramexicana*(A.Gray)Borhidi | Aerialparts | GC-5269/8 | 75.09±6.62 | 79.20±8.23 |
| Rutaceae | | | | |
| *Casimiroaedulis*LaLlave | Leaves | GC-5198/15 | 57.03±11.41 | 99.63±6.42 |
| | Stembark | GC-5198/15 | 59.47±1.81 | 90.93±2.02 |
| *Pilocarpusracemosus*Vahl | Leaves | GC-5235/3 | 47.84±6.63 | 85.21±2.73 |
| | Stembark | GC-5235/3 | 83.14±11.24 | 91.66±2.49 |
| *Zanthoxylumfagarasubsp.aguilarii*(Standl.& Steyerm.)Reynel | Aerialparts | GC-4796/4 | 41.57±3.84 | 74.23±6.62 |
| Salicaceae | | | | |
| *Caseariacorymbosa*Kunth | Stembark | GC-5170/9 | 29.39±6.91 | 79.24±9.74 |
| | Leaves | GC-5222/15 | 1.12±0.12 | 82.70±12.32 |
| *Pipareadentata*Aubl. | Aerialparts | GC-5239 | 1.06±0.22 | 77.96±7.46 |
| *Prockiacrucis*P.BrowneexL. | Aerialparts | GC-5171/4 | 67.80±5.96 | 78.54±3.75 |
| *Xylosmaflexuosa*(Kunth)Hemsl. | Leaves | GC-4900/7 | 40.29±11.84 | 74.52±8.26 |
| | Aerialparts | GC-5231/3 | 86.68±3.26 | 97.64±11.39 |
| *Xylosmavelutina*(Tul.)Triana&Planch. | Aerialparts | GC-5318/4 | 61.39±11.75 | 75.68±8.20 |
| Sapindaceae | | | | |
| *Paulliniacururu*L. | Aerialparts | GC-5320/4 | 52.14±4.02 | 78.64±10.70 |
| Solanaceae | | | | |
| *Browalliaamericana*L. | Aerialparts | GC-5133/4 | 73.38±5.64 | 83.14±4.41 |
| *Lycianthesarrazolensis*(Coult.&Donn.Sm.)Bitter | Leaves | GC-5337/4 | 72.95±10.72 | 74.59±5.19 |
| *Solanumnudum*Dunal | Leaves | GC-4969/8 | 56.63±5.80 | 71.29±2.25 |
| | Fruit | GC-4969/8 | 8.36±4.80 | 88.76±1.33 |
| Viburnaceae | | | | |
| *Viburnumhartwegii*Benth. | Leaves | JM-5196/11 | 68.53±13.61 | 94.51±5.84 |
| | Stembark | JM-5196/11 | 83.43±7.06 | 103.83±1.17 |

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Antitrypanosome Screening of Crude Extracts: With a few adjustments, the antitrypanosome luminescence test was carried out in accordance with Castillo et al. 2022 5. 50 µL of Trypanosoma cruzi epimastigotes (strain CL-Brener) at a concentration of 9x105 suspended in GIT medium supplemented with hemin (5 mg/500 mL) and 10% inactivated fetal bovine serum were added to white 384-well plates (Optiplate, Perkin Elmer). These were cultured for 24 hours at 28°C after the addition of 0.5 µL of plant extracts in DMSO at doses of 10 and 1 mg/mL. Every extract was assessed three times. GIT media without epimastigotes, GIT medium with parasites + DMSO, and GIT medium with DMSO were used as blanks, while benznidazole and tamoxifen (10 mM, 5 mM, 1.25 mM, and 0.25 mM) were used as positive controls. Following incubation, each well received 20 µl of Cell Titer-Glo®2.0 reagent (PROMEGA), which was then incubated for 15 minutes at 28°C under light protection. A Biotek Synergy HTX multimode plate reader was used to quantify luminosity at 28°C. Table 1 displays the findings in terms of viability percentage.
RESULTS: The 127 methanolic dried extracts from 114 plant species that were obtained were used for the antitrypanosomal screening (Table 1).

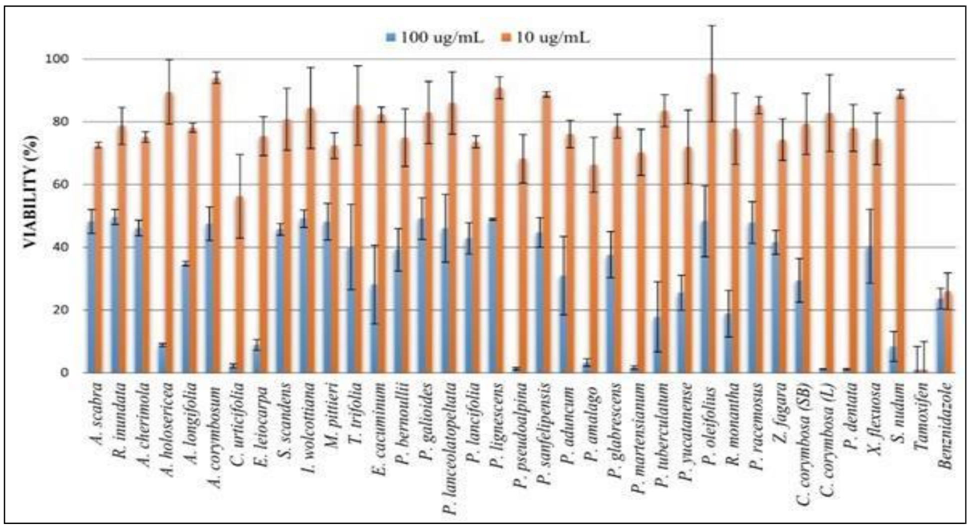


**FIG.1:ANTITRYPANOSOMALACTIVITYOFSALVADORANACTIVESPECIESAGAINSTEPIMASTIGOTE STAGE OF *TRYPANOSOMA CRUZI***

4.6–17.9%, entire plant 6.2–20.7%, stembark 4.3–22.1%, branches 2.3–4.8%, fruits 10.4–16.9%, and roots 3.5 percent were the yields from extracts of aerial parts. Table 1 provides a summary of the antitrypanosomal screening activity represented in viability percent. 34 species from 14 botanic families were deemed active (less than 50% of viability percent at 100 µg/mL) based on prior criteria 5 (Fig. 1). The greatest number of active botanical species were found in the groups Piperaceae, Asteraceae, Salicaceae, Annonaceae, and Acanthaceae (Fig. 2). The organs and components of the active plants that shown activity were the aerial parts (43%), leaves (34%), and whole plant (14%), with stem bark (6%) and fruits (3%), following closely behind. Table 1.

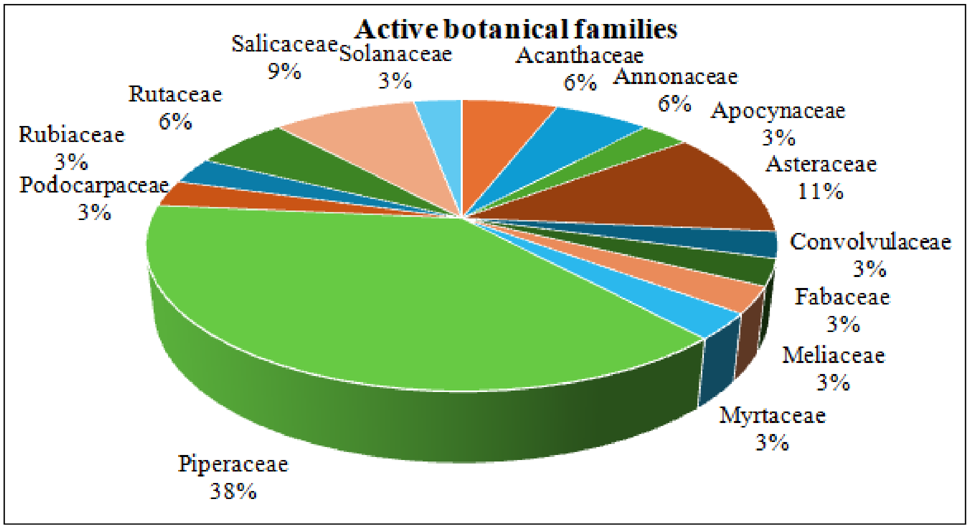


**FIG.2:ACTIVESALVADORANBOTANICALFAMILIESAGAINSTEPIMASTIGOTESOF*TRYPANOSOMA CRUZI* (VIALIBILITY < 50%)**

DISCUSSION: Of the 34 active species found, only nine showed exceptional activity against T. cruzi epimastigote, with over 90% reduction of epimastigote viability at 100 µg/mL. Table 2 and Figure 1. Of these, Table 2 shows that Annona holosericea (Annonaceae) has a 91.18±0.52% aviability suppression at 100 µg/mL. Numerous biological activities, including antineoplastic, antiparasitic, cytotoxic, antitumoral, antiprotozoal, antidiabetic, and anti-inflammatory properties, are known to be present in the Annonaceae family, and more especially in the genus Annona.

analgesic and hepatoprotective qualities 7, 8, 9. Studies explicitly addressing A. holosericea's antitrypanosomal activities are nonexistent. But historically, A. crassiflora has been utilized to treat Chagas disease 10,11. Furthermore, some studies indicate that alkaloids, acetogenins, and terpenes are responsible for antitrypanosomal activity, and other reports indicate that A. foetida, A. crassiflora, A. muricata, A. squamosa, A. haematantha, A. purpurea, A. coriacea, and A. senegalensis are active against T. cruzi 12,7,4.

**TABLE2:SALVADORANSPECIESWITHPROMINENTANTITRYPANOSOMALACTIVITYAGAINSTEPIMASTIGOTE STAGE OF *TRYPANOSOMA CRUZI***

| Family/Scientificname | Vernacularname | Plantpartused | Viabilitysuppression(%)at100µg/mL[2] |
|---|---|---|---|
| **Annonaceae** | | | |
| *Annonaholosericea*Saff. | "Sincuyita" | Stembark | 91.18±0.52 |
| **Asteraceae** | | | |
| *Caleaurticifolia*DC. | "Juanislama" | Leaves | 97.83±0.65 |
| *Eremosisleiocarpa*(DC.) Gleason | "Palodelasma" | Aerialparts | 91.18±1.71 |
| **Piperaceae** | | | |
| *Peperomiapseudoalpina*Trel. | "Hojadetrespiedras" | Wholeplant | 98.75±0.35 |
| *Piperamalago*L | "SantaMaría" | Leaves | 96.78±1.20 |
| *Pipermartensianum*C. DC. | "Candelillo" | Aerialparts | 98.38±0.50 |
| **Salicaceae** | | | |
| *Caseariacorymbosa*Kunth | "Canjurillo" | Leaves | 98.88±0.12 |
| *Pipareadentata*Aubl. | "Camarónrojo" | Aerialparts | 98.94±0.22 |
| **Solanaceae** | | | |
| *Solanumnudum*Dunal | "Palodelgolpe" | Fruit | 91.64±4.80 |

The World Flora Online lists the following scientific names: http://www.worldfloraonline.org (July 7th, 2024). Three replicates ± standard deviations (SD) are used to illustrate the viability suppressions.

There are several subfamilies, genera, and species within the Asteraceae family, with plants and shrubs being the most prevalent; this family is characteristic of trypanocidal action 13,1415. which has antiparasitic properties linked to alkaloids, flavonoids, phenolic acids, coumarins, terpenoids, quinolines and diterpenoids, triterpenoid sesquiterpene lactones, and pyrethrins 15.

According to our findings, Calea urticifolia, also known as "Juanislama" in El Salvador, had significant efficacy (viability suppression at 100 µg/mL:97.83±0.65%) against stepimastigotes (Table 2). This species is used as a bactericide and to heal stomach ulcers. Sesquiterpene lactones (germacranolides and heliangolides), some phenols, isoeugenol, and derivatives of phloroglucinol have been isolated as a consequence of various investigations into C. urticifolia 17, 18, 19, and 14.
The presence of phenolic compounds and sesquiterpene lactones may be the cause of this, the first report of antitrypanosomal action for C. urticifolia 15. However, C. uniflora has shown in vitro efficacy against T. cruzi's trypomastigote form 20, 21, 22.
Eremosis leiocarpa, formerly called as Vernonia leiocarpa (viability suppression at 100 µg/mL:91.18±1.71%), is used in El Salvador to treat asthma 23. There are no reports of antitrypanosome activity in Table 2, however E. leiocarpa 24 included some sesquiterpene lactones (glaucolide F, G, and H) that may be interesting antitrypanosomal chemicals. Additionally, members of this genus, such as V. auriculifera, V. brasiliana, V. guineensis, V. subuligera, V. polyanthes, and V. scorpioides, have been discovered as sources of trypanocidal chemicals 23, 25.
Peperomia pseudoalpina (viability suppression at 100 µg/mL: 98.75±0.35%), Piper amalago (viability suppression at 100 µg/mL: 96.78±1.20%), and P. martensianum (viability suppression at 100 µg/mL: 98.38±0.50%) were among the Piperaceae species that exhibited the strongest antitrypanosomal activity, according to Table 2. Traditional medicine uses this family of plants to treat a variety of illnesses, including protozoal diseases. They are also known to contain secondary metabolites that have antitrypanosomal, antileishmanial, anxiolytic, anticonvulsant, and anti-inflammatory properties (26, 27, 5).
Peperomia pseudoalpina has been understudied despite its biological significance and strong antitrypanosomal action. Similarly, there is currently no information on the phytochemical and biological screening in the literature. Additionally, reports of similar behavior have been made for several Peperomia species. 5, 6. Furthermore, certain bioactive substances were shown to have trypanocide action against trypomasti and stepimastigote. goteofT.cruzi, including lignans 29, 30, and 6.
Similar to phenylpropanoids, tetrahydrofuran lignans are thought to be the cause of the action in Peperomia. Anti-inflammatory, antibacterial, cicatrizing, antioxidant, and antileishmanial are among the pharmacological qualities of P. amalago 31, 32. Its phytochemical roots are mostly composed of isobutylamides, pyrrolidines, and sesquiterpenes. 31. When tested against Leishmania amazonensis promastigotes, two pyrrolidine alkaloids—N-[7- (3', 4'-methylenedioxyphenyl) - 2(E), 4(E)- heptadienoyl] pyrrolidine and N-[7-(3', 4'-methylenedioxyphenyl)-2(Z), 4(Z)-heptadienoyl] pyrrolidine—showed encouraging results 27. Furthermore, a derivative drug was tested against T. cruzi 31's stepimastigote and amastigote forms. This is the first report of biological activity ascribed to P. martensianum, since there are no publications of its phytochemical composition or biological activities. Its potential effect may be linked to flavonoids and derivatives of benzoic acid, as earlier investigations of the Piper species have shown (28, 26, 5).
The Salicaceae family includes the genus Casearia, which has long been used as a topical anesthetic, anti-inflammatory, antiophidic, antipyretic, and antiseptic 33 as well as for gastrointestinal diseases and wound healing. The second most active species against T. cruzi epimastigotes is C. corymbosa, which suppresses 98.88% of viability at 100 µg/mL (Table 2). Some diterpenoids, including clerodane, labdane, kaurene, kolovane types, γ-sitosterol, and phenolic acids, have been isolated from its leaves and bark 34, 35, 36. The antitrypanosomal action of C. corymbose-like Piparea dentata (formerly known as Casearia commersoniana) has not yet been fully explored, despite its intriguing chemical makeup. Its suitability for these kinds of investigations is supported by the fact that Casearia sylvestris, a different species from the same genus, has been shown to have antitrypanosomal action against T. cruzi 37.
According to Table 2, the extract from P. dentata's aerial parts was the most effective in this investigation, decreasing the 98.94% vitality of T. cruzi epimastigotes at 100 µg/mL. Although goat poisoning from its fruits has been documented 38, this is the first evidence of biological action. As a result, before conducting phytochemical and biological research on this species, toxicity studies should be conducted. Traditional medicine uses fruits of the Solanum nudum (Solanaceae) family (viability suppression at 100 µg/mL:91.64±4.80%, Table 2) to treat fevers 39. Several steroids and sapogenins have been isolated 40, 39,

41, 42, some of which showed antiplasmodial or antimalarial activity, and none of them were found to be mutagenic, clastogenic, or cytotoxic. 39, 41, 42. Since many Solanum species' unripe fruits are harmful to humans, toxicology tests are advised. 43. RESULTS: It is noteworthy to emphasize the significant activity of 9 species (viability suppression > 90%) out of the 114 examined species, 34 of which were active against T. cruzi epimastigotes. Based on their toxicity, biological activity, and chemical makeup, Casearia corymbosa, Peperomia pseudoalpina, and Piper martensianum are the most promising species. As a result, these species could be good places to find novel chemicals that might be used to treat Chagas disease. This demonstrates that antitrypanosomal species and antikinetoplastid agents are increasingly found in Salvadoran flora.

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