**Supplementary Table 1:** Examples of virtual screening techniques applied for trypanosomiasis and leishmaniasis drug development.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***T. cruzi*** | | | | | |
| **Target** | **Drug/Compound** | **Ref** | **Target** | **Drug/Compound** | **Ref** |
| Polyamine transporter | Isotretionin | [Reigada *et al.*, 2017](#_ENREF_36) | Cruzain  (cruzipain) | N-acylhydrazone derivatives | [Herrera-Mayorga *et al.*, 2019](#_ENREF_16) |
| Triclabendazole  Sertaconazole  Paroxetine | [Alberca *et al.*, 2016](#_ENREF_2) | Amiodarone Bromocriptine | [Bellera *et al.*, 2013](#_ENREF_4) |
| Cinnarizine  Clofazimine | [Alberca *et al.*, 2018](#_ENREF_3) | Levothyroxine | [Bellera *et al.*, 2014](#_ENREF_5) |
| Cisapride | [Dietrich *et al.*, 2018](#_ENREF_12) | Etofylline clofibrate  Piperacillin  Cefoperazone  Flucloxacillin | [Palos *et al.*, 2017](#_ENREF_31) |
| Promazine, Chlorpromazine Clomipramine | [Reigada *et al.*, 2019](#_ENREF_35) | 2-acetamidothiophene-3-carboxamide | [Wiggers *et al.*, 2013](#_ENREF_47) |
| Proline transporter | Loratadine, Cyproheptadine Clofazimine | [Saye *et al.*, 2020](#_ENREF_39) | Carbamoyl -imidazoles | [de Souza *et al.*, 2019](#_ENREF_10) |
| Sirtuin2 | Nicotinamida | [Soares *et al.*, 2012](#_ENREF_42) | NSC227186  NSC67436  NSC260594 | [Rogers *et al.*, 2012](#_ENREF_37) |
| Proline racemases | OxoPA  Br-OxoPA | [Berneman *et al.*, 2013](#_ENREF_6) | Dihydroorotate dehydrogenase class 1A | V4 | [Cheleski *et al.*, 2010](#_ENREF_8) |
| Arginine kinase | Resveratrol | [Valera Vera *et al.*, 2016](#_ENREF_46) | Glyceraldehyde-3-phosphate-dehydrogenase | 4-amino-thiophen derivative  1,3-dioxoisoindoline derivative  1-pyrazolyl-ethanone derivative | [Maluf *et al.*, 2013](#_ENREF_23) |
| AKT-like Kinase | Pyrazolopyrimidine structural analogue | [Ochoa *et al.*, 2018](#_ENREF_29) | Dihydroindole compounds | [Prokopczyk *et al.*, 2014](#_ENREF_33) |
| Trans-Sialidase | Sulfasalazine | [Lara-Ramirez *et al.*, 2017](#_ENREF_21) | Carbonic anhydrase | 8 compounds | [Llanos *et al.*, 2020](#_ENREF_22) |
| Trypanothione  reductase | Chlorhexidine derivatives  Piperidine derivative | [Meiering *et al.*, 2005](#_ENREF_25) | Phosphodiesterase C | ZLN55, ZLN66, ZLN68,  ZLN82 | * [King-Keller *et al.*, 2010](#_ENREF_20) |
| ***T. brucei*** | | | | | |
| **Target** | **Drug/Compound** | **Ref** | **Target** | **Drug/Compound** | **Ref** |
| Ornithine  decarboxylase | Benzthiazoles, Alexidine  Dithioamidines | [Smithson *et al.*, 2010](#_ENREF_41) | Bromodomain factor 2 | GSK2801 | [Yang *et al.*, 2017](#_ENREF_48) |
| RNA Editing Ligase 1 | Naphthalene derivatives | [Durrant *et al.*, 2010](#_ENREF_13) | Glyceraldehyde-3-  phosphate-  dehydrogenase | Geranylated -benzophenone derivatives | [Herrmann *et al.*, 2015](#_ENREF_17) |
| GlcNAc-PI de-  N-acetylase | Ethambutol  metaraminol | [Rashmi & Swati, 2015](#_ENREF_34) | 6-phospho  Gluconate-  dehydrogenase | Six new scaffolds | [Ruda *et al.*, 2010](#_ENREF_38) |
| RNA-editing Terminal Uridylyl Transferase 2 | 20 scaffolds | [Demir *et al.*, 2014](#_ENREF_11) | Pteridine reductase 1 | Benzo[d]imidazol-2-amine derivatives | * [Mpamhanga *et al.*, 2009](#_ENREF_27); [Spinks *et al.*, 2011](#_ENREF_43) |
| ***Leishmania spp.*** | | | | | |
| **Target** | **Drug/Compound** | **Ref** | **Target** | **Drug/Compound** | **Ref** |
| Dihydroorotate dehydrogenase | Natural products from Asteraceae species | [Chibli *et al.*, 2018](#_ENREF_9) | Glucosidase-like protein | Miglitol | [Chavez-Fumagalli *et al.*, 2019](#_ENREF_7) |
| 3MJYcZ01 | [Ochoa *et al.*, 2016](#_ENREF_30) | γ-Glutamylcysteine synthetase | BTB13337, BTB13334, HTS05833, HTS11169 | [Agnihotri *et al.*, 2017](#_ENREF_1) |
| Phosphodiesterase | Phenylfuranchalcones | [Ochoa *et al.*, 2019](#_ENREF_28) | *S*-adenosyl-l-homocysteinease (AdoHcyase) | Synthetic compound | [Khare *et al.*, 2012](#_ENREF_19) |
| Translation initiation  factor 4A | 6-α-aminocholestanol | [Harigua-Souiai *et al.*, 2018](#_ENREF_15) | Arginase | N-acylhydrazones | [Stevanovic *et al.*, 2019](#_ENREF_45) |
| Type 2 NADH dehydrogenase | 6-methoxy-quinalidine | [Stevanovic *et al.*, 2018](#_ENREF_44) | Pyruvate phosphate dikinase | Z220582104 | [Kashif *et al.*, 2019](#_ENREF_18) |
| Nucleoside diphosphate kinase | BTB13319 | [Mishra *et al.*, 2017](#_ENREF_26) | Ascorbate peroxidase | ASN13153257, ASN16457210 AOP22837786 | [Mansuri *et al.*, 2017](#_ENREF_24) |
| Dipeptidylcarboxy-peptidase | (2Z,2′Z)‐3,3′‐(ethane‐1,2‐diylbis(azanediyl))bis(1‐(4‐halophenyl)‐6‐hydroxyhex‐2‐en‐1‐one) derivatives  3,5‐disubstituted isoxazole derivative | [Gangwar *et al.*, 2012](#_ENREF_14) | Lipase LdLip3 | ZINC01821375 ZINC04008765 ZINC06117316  ZINC12653571 | [Parameswaran *et al.*, 2014](#_ENREF_32) |
| L-asparaginase I | ZINC 565127 | [Singh *et al.*, 2015](#_ENREF_40) |  |  |  |