

## Patent Annotations:

The patents annotated in this section have been selected by the authors of this issue as the most important patents of relevance to their field.

### RECENT PATENTS ON TREATMENT OF SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

1. **SARS CoV main protease inhibitors**, Wu, S.-Y., Hsieh, H.-P., Hsu, T.-A., Lu, I.-L.: *US2006019967A1* (2006).

#### Commentary:

Dicyclic or multi-cyclic compounds inhibit the activity of severe acute respiratory syndrome (SARS) coronavirus (CoV) main protease and hepatitis C virus.

2. **Inhibitors of severe acute respiratory syndrome (SARS) 3C-like proteinase**, Fuhrman, S., Matthews, D.A., Patick, A.K., Rejto, P.: *US2004235952A1* (2004).
3. **Inhibitors of SARS 3C like protease**, He, M., Kania, R.S., Lou, J., Planken, S.: *US2006014821A1* (2006).

#### Commentary:

The invention relates to SARS-related coronavirus 3C-like proteinase with an effective amount of a rhinovirus 3C-like protease inhibitor which is used in inhibiting Severe Acute Respiratory Syndrome (SARS) viral replication.

4. **SARS coronavirus 3CL protease inhibitor and its use**, Lai, L., Liu, Y., Fan, K.: *CN1569841A* (2005).

#### Commentary:

The invention discusses a SARS coronavirus 3CL protease inhibitor and its use for the prevention and treatment of SARS virus.

5. **Baicalin and its derivatives as a treatment for SARS coronavirus infection or other related infections**, Yuen, K., Chen, F., Chan, K.: *WO05044281A1* (2005).

#### Commentary:

This invention identifies a pharmaceutical composition comprising of baicalin, a naturally occurring compound extracted and purified from the Chinese medicinal plant *Scutellaria baicalensis* Georgi, used for the treatment of diseases associated with viruses of family *Coronaviridae*, such as Severe Acute Respiratory Syndrome (SARS).

6. **The severe acute respiratory syndrome coronavirus**, Rappuoli, R., Masignani, V., Stadler, K., Gregersen, J.-P., Chien, D., Han, J., Polo, J., Weiner, A., Houghton, M., Song, H.C., Seo, M.Y., Donnelly, J.J., Klenk, H.D., Valiante, N.: *WO04092360A2* and *WO04092360A3* (2004).

#### Commentary:

The present invention discusses nucleic acids and proteins which are useful in the preparation and manufacture of vaccine formulations that can inactivate (or kill) Severe

Acute Respiratory Syndrome (SARS) virus for the treatment or prevention of SARS.

### ANTIBIOTIC TREATMENT STRATEGIES FOR *HELICOBACTER PYLORI* INFECTION

1. **Mutilins for the treatment of disorders caused by *Helicobacter pylori***, Ascher, G., Hildebrandt, J.: *WO03090740* (2003).

#### Commentary:

The present invention discusses a method of preventing or treating diseases mediated by *Helicobacter pylori* by using an effective amount of a pleuromutilin.

2. **Methods and compositions for the treatment of *Helicobacter pylori*-associated diseases using endoperoxide bridge-containing compounds**, Marash, M., Kluev, E.: *WO05048912A2* and *WO05048912A3* (2005).

#### Commentary:

The present invention relates to methods and compositions for treating pathological conditions associated with *Helicobacter pylori* in which high intracellular ferrous iron concentration is required for their survival and pathogenesis. The invention comprises of endoperoxide bridge-containing compounds that helps in the eradication and inhibition of the growth of the ferrous-dependent bacteria. The compositions also include at least one active agent for treating *Helicobacter pylori*-related gastrointestinal disorders, such as a proton pump inhibitor, an H2 blocker or a bismuth-containing compound.

### AN INSIGHT ON TARGETS AND PATENTED DRUGS FOR CHEMOTHERAPY OF CHAGAS DISEASE: A REVIEW

1. **Compounds, compositions and methods for treatment of parasitic infections**, Lim-Wilb, M., Semple, J.E., Araldi, G.L., Goldman, E.A., Weinhouse, M.I.: *WO0248097A1*, *WO0248097B1* and *WO0248097C2* (2003).

#### Commentary:

This invention provides pharmaceutical compositions containing acrylate, acryl-amide, -ketoamide and aldehyde derivatives of peptides, useful as antiparasitic agents, particularly in the treatment, prevention or amelioration of Chagas disease. Methods for modulating the activity of cruzipain, compounds and compositions, without specific biological data are also available.

2. **Inhibitors of cruzipain and other cysteine proteases**, Quibell, M., Ramjee, M.K.: *US20056958358* (2005).

**Commentary:**

A group of amide compounds inhibiting cruzipain more efficiently than some mammalian CPs, such as human Cathepsins L and K, is described. These compounds are used as therapeutic agents for Chagas disease.

- Heteroaryl nitrile derivatives**, Altman, E., Betschart, C., Hayakawa, K., Irie, O., Sakaki, J., Iwasaki, G., Lattmann, R., Missbach, M., Teno, N.: WO04020441A1 (2004).

**Commentary:**

This invention relates to peptidic inhibitors of cysteine proteases, in particular to heteroaryl nitrite Cathepsin K inhibitors, used for the treatment of osteoporosis and several parasitic diseases including Chagas disease.

- Protease inhibitors**, Bondebjerg, J., Fuglsang, H., Naerum, L.: WO04110988A1 (2004).

**Commentary:**

This patent relates to cysteine protease inhibitors which are useful in the treatment and prevention of some diseases in which proteases are involved, especially mast cell mediated inflammatory diseases. The invention relates to peptidyl nitriles capable of selectively inhibiting dipeptidylpeptidase I (DPPI), also known as cathepsin C. A compound of this invention is useful for the treatment of a variety of diseases including Chagas disease.

- Nitriles useful as reversible inhibitors of cysteine proteases**, Hickey, E.R., Bekkali, Y., Patel, U.R., Spero, D.M., Thomson, D.S., Young, E.R.: US20066982263 (2006).

**Commentary:**

Novel synthetic nitrile compounds are reversible inhibitors of cysteine proteases such as cathepsins K, S, F, L and B. They are used for treating diseases caused by these proteases such as osteoporosis, rheumatoid arthritis, multiple sclerosis, asthma and other autoimmune diseases, Alzheimer's disease, and atherosclerosis.

- Thiosemicarbazone and semicarbazone inhibitors of cysteine proteases and methods of their use**, Cohen, F.E., Du, X., Guo, Ch., McKerrow, J.H.: US20056897240 (2005).

**Commentary:**

The present invention relates to thiosemicarbazone and semicarbazone inhibitors of cysteine proteases and methods of using such compounds to prevent and treat protozoan infections such as trypanosomiasis, malaria and leishmaniasis.

- Methods related to metabolism of parasites and mycobacteria**, Prestwich, G.D., Buckner, F.S., Hinshaw, J.C.: WO0076316A1 (2000).

**Commentary:**

Sterol biosynthesis has been studied extensively in mammals, eubacteria and yeast compared to parasites and mycobacteria. The present invention provides methods to inhibit

the physical development of *T. cruzi*, affecting parasitic oxidosqualene cyclase activity of the parasite. Results of *in vivo* and *in vitro* assays show the outstanding potency of the oxidosqualene cyclase inhibitors.

- Compounds and methods for the inhibition of *Trypanosoma cruzi***, Hamilton, A.D., Van Voorhis, W.C., Yokoyama, K., Buckner, F.S., Ohkanda, J., Gelb, M.: WO03006012A1 (2003) and BR0211098A (2004).

**Commentary:**

This invention includes a group of compounds and methods for treating infections caused by protozoal, fungal and/or bacterial agents such as *Trypanosoma cruzi*. It also provides pharmaceutical compositions for the treatment of microbial infections, including protozoal infections such as Chagas disease. Data of mice survival suggests the inhibition of C-14 demethylase involved in the antiparasitic activity.

- Platinum (II) compounds**, Lowe G.: WO0050431A1 (2000).

**Commentary:**

Platinum compounds are described in this patent which are used in the treatment of the human or animal body. In particular, the invention relates to 2,2':6',2"-terpyridine platinum (II) compounds used as anti-protozoal, anti-rheumatoid arthritis or anti-tumor agents.

- Dihydrofolate reductase inhibitors**, Lowe G.: WO0153276A1 (2001).

**Commentary:**

The present invention relates to triazine derivatives acting as dihydrofolate reductase inhibitors and their use as antiparasitic agents, for example against *T. cruzi*.

- Nucleoside pyrophosphate and triphosphate analogs and related compounds as therapeutic agents**, Bottaro, J.C., Schmitt, R.J., Petrie, M.A., Penwell, P.E.: WO0114401A1 (2001).

**Commentary:**

In the nucleoside pyrophosphate and triphosphate analogs, the pyrophosphate or triphosphate group is replaced with a moiety which is hydrolytically and enzymatically more stable. These compounds are useful as therapeutic agents, e.g., as antiviral agents, anticancer agents, metabolic moderators and protozoal infectious diseases including Chagas disease. It also provides pharmaceutical compositions and methods for treatment.

- Use of inhibitors of the sodium-hydrogen exchanger for the production of a pharmaceutical for the treatment of disorders which are caused by protozoa**, Lang, H.J., Lanzer, M., Wiesner, J., Sanchez, C., Wunsch.: US20006114393 (2000).

**Commentary:**

Guanidine derivative compounds are described as being Na<sup>+</sup>/H<sup>+</sup> exchange inhibitors which are useful for the treatment of protozoal infections including Chagas disease.

13. **Use of canthin-6-one, plant extracts containing same and derivatives thereof in the treatment of trypanosomiasis, Ferreira, M.E., Fournet, A., Rojas de Arias, A., Hocquemiller, R., Poupon, E.: WO04050092 A1 and WO04050092B1 (2004).**

**Commentary:**

Canthin-6-one and derivatives obtained from plant extracts of *Zanthoxylum chiloperone* are used for the treatment of trypanosomiasis, particularly *T. cruzi* infection. These natural compounds are assayed in chronic and acute mouse models more effectively than benznidazole.

14. **Process to obtain dibenzylbutyrolactonic lignans; process to obtain synthetic derivatives from lignans bearing anti-Chagas chemoprophylactic and therapeutic activities, Silva, M.L.A., Albuquerque, S., Souza, G.E.B., Bastos, J.K., Silva, R.: WO03080600A1 (2003).**

**Commentary:**

The invention relates to a process to obtain lignans, especially cubebin and methylpluviatolide, from leaves of *Zanthoxylum naranjillo* or *Piper cubeba*. It also refers to a process to obtain semi-synthetic derivatives of cubebin, especially dibenzylbutyrolactonic lignans, such as: hinokinin, o-acetyl cubebin, o-methyl cubebin, 6,6'-dinitrohinokinin and o-dimethylethylamine cubebin and other derivatives. These compounds are used to manufacture drugs which are useful for the treatment and prophylaxis of Chagas disease.

15. **Antiprotozoal imidazopyridine compounds, Wyvratt, M.J., Biftu, T., Fisher, M.H., Schmatz, D.M.: WO04080390A2 and WO04080390A3 (2004).**

**Commentary:**

Imidazopyridine or N-oxides derivative compounds are described in the present invention as being useful for the treatment and prevention of protozoal diseases in mammals and birds. Methods for the treatment and prevention of some mammalian protozoal diseases, including Chagas disease, are also provided. However, these compounds are reported as useful especially for coccidiosis.

**NOVEL THERAPIES FOR CYTOMEGALOVIRUS DISEASE**

1. **RNAi targeting of viruses, Kowalik, T.F.: US20040248839A1 (2004).**

**Commentary:**

Pharmaceutical methods and compositions which inhibit viral proliferation and replication in cytomegalovirus (CMV) infection in non-human primates or in humans comprise of a siRNA or vector expressing siRNA, and a pharmaceutically acceptable carrier.

**LINEZOLID IN CHILDREN: RECENT PATENTS AND ADVANCES**

1. **Topical hydro-alcoholic formulations of oxazolidinone antibacterial agents, Pena, L.E., Secreast, P.J.: WO06059221A3 (2006).**

**Commentary:**

The present invention relates to a hydro-alcoholic formulation comprising of oxazolidinone antibacterial agent, such as linezolid, dissolved in a mixture of water and a monohydric non-aromatic alcohol of one to seven carbon atoms, such as ethanol or isopropanol which are suitable for topical administration. These formulations are used for the treatment and prevention of bacterial infections.

2. **Oxazolidinone derivatives with antibiotic activity, Gravestock, M.B., Betts, M.J., Matthews, I.R., Griffin, D.A.: US20067141583 (2006).**

**Commentary:**

The present invention discusses antibiotic compounds that contain a substituted oxazolidinone ring and are used as therapeutic agents.

3. **Modulators of ribosomal function and identification thereof, Steitz, T.A., Moore, P.B., Ban, N., Nissen, P., Hansen, J.: US2006136146A1 (2006).**

**Commentary:**

The invention provides methods for producing high-resolution crystals of ribosomes and ribosomal subunits in combination with protein synthesis inhibitors which are specifically designed to kill or inhibit the growth of any target organism.

4. **Novel intermediates for linezolid and related compounds, Mohan, R.D., Krishna, R.P.: US20060247435A1 (2006).**

**Commentary:**

The present invention identifies novel processes for the preparation of 5-aminomethyl-substituted oxazolidinones, key intermediates for oxazolidinone antibacterials including linezolid.

5. **Solid forms of linezolid and processes for preparation thereof, Aronhime J., Koltai, T., Braude, V., Fine, S., Niddam, T.: WO06110155A1 (2006).**

**Commentary:**

The novel crystalline forms of linezolid are characterized by powder X-ray diffraction, FTIR and FTRaman spectroscopy, and differential scanning calorimetry. The pharmaceutical compositions comprising these compounds, are used to treat gram-positive bacterial infections.

**MEDICATION ASSISTED TREATMENT OF DRUG ABUSE AND DEPENDENCE: GLOBAL AVAILABILITY AND UTILIZATION**

1. **Heterocyclic carboxamide compounds effective in the treatment of drug abuse, Bohme, A., Dubroeuq, M.-C., Fratta, W., Guyon, C., Imperato, A., Manfre, F.: US20006150387 (2000).**

**Commentary:**

Heterocyclic carboxamide compounds are used for preventing or reducing self-administration or overuse of a drug or a substance capable of giving rise to pharmacomania by a human or animal patient. The preferred drugs or

substances are nicotine, caffeine, benzodiazepines, narcotics, and hallucinogens.

2. **Method of simultaneously enhancing analgesic potency and attenuating dependence liability caused by morphine and other bimodally-acting opioid agonists, Crain, S.M., Shen, K.-F.: US20067026329 (2006).**

**Commentary:**

This present invention relates to a method for enhancing analgesic potency of an opioid agonist such as morphine, while attenuating anti-analgesia, hyperalgesia, hyperexcitability, physical dependence and/or tolerance (excitatory) effects associated with the chronic use of bimodally-acting opioid agonist.

3. **Substituted furo[2,3-b]pyridine derivatives, Toupençe, R.B., Debenham, J.S., Goulet, M.T., Madsen-Duggan, C.B., Walsh, T.F., Shah, S.K.: US20067091216 (2006).**

**Commentary:**

The novel substituted furo[2,3-b]pyridine derivatives are antagonists of the Cannabinoid-1 (CB1) receptor, useful in the prevention and treatment of diseases mediated by the

cannabinoid-1 (CB1) receptor. These compounds act as mediators in the treatment of psychosis, memory deficits, cognitive disorders, migraine, neuropathy, neuroinflammatory disorders including multiple sclerosis and Guillain-Barre syndrome and the inflammatory sequelae of viral encephalitis, cerebral vascular accidents, and head trauma, anxiety disorders, stress, epilepsy, Parkinson's disease, movement disorders, and schizophrenia. These compounds are also useful for the treatment of substance abuse disorders, obesity or eating disorders associated with excessive food intake, cirrhosis of the liver and asthma.

4. **Combination of desoxypeganine and mecamlanine for the treatment of alcohol abuse, Moormann, J., Opitz, K., Winterhopff, H.: US2006199866A1 (2006).**

**Commentary:**

The present invention identifies an active substance combination having deoxypeganine or one of its pharmaceutically acceptable derivatives, and mecamlanine or one of its pharmaceutically acceptable derivatives. This composition is used to produce a medicament for the treatment of alcohol abuse and/or alcohol dependence.