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A Review on Suramin- Fruit of Early Medicinal Chemistry

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ABSTRACT:

An old medication called suramin is used to treat river blindness and the first stage of acute human sleeping sickness brought on by the trypanosome brucei rhodesiense. Suramin exerts its effects independently of the central nervous system. Suramin exhibits negative effects. Suramin is a chemical with numerous uses. It is possible to identify a less hazardous molecule for a variety of suramin applications. In this audit Suramin is typically used to treat the African illness known as sleeping sickness, but it also exhibits promise as an antiviral, anticancer, antidote, and antiviral medication. The principle point of audit is to likely grown use of suramin. The mechanism of action of suramin is unknown. This study is on different disease such as cancer, autism, snake venom, viral from this review we resume that the treatmemt of suramin drug on cancer, autism, snake venom, viral is give positive effect but also show some adverse effect. suramin is still under debate. we don't know exactly that suramin is harmful or is it a shield. Further researches and clinical trial on suramin is continous for better effect of suramin.

Keywords- Trypanosomabrucei,suramin,polypharmacology,sleepingsickness,intravenous

1. Introduction

The 100-year-old medication suramin is used to treat river blindness and the first stage of the African sleeping sickness. It is the preferred method of treatment for sleeping illnesses that do not involve the central nervous system, but it has a reasonable amount of side effects.

Paul Ehrlich created the dye trypan blue in 1904, and Bayer went on to create a number of colourless, more effective compounds based on its antitrypanosomal properties. Suramin was in molecule 205. A polysulfonatednaphthylamine is suramin

The chemists Oskar Dressel, Richard Kothe, and Bernhard Heymann developed suramin for the first time at the Bayer AG facilities in Elberfeld after studying a number of urea-like chemicals. Bayer continues to market the medication under the trade name Germanin

Due to Bayer's commercial and strategic interests, the chemical structure of suramin was kept a secret; however, Ernest Fourneau and his team at the Pasteur Institute clarified and published it in 1924.378–379

as least as early as 1916, suramin was produced. It is listed as one of the Essential Medicines by the World Health Organization [6] [2]. It can be obtained through the Centers for Disease Control in the United States (CDC) [1].

Suramin is used to treat trypanosome-related human sleeping sickness. It is used to treat first-stage African trypanosomiasis without affecting the central nervous system, specifically caused by Trypanosomabruceirhodesiense and Trypanosomabruceigambiense.[8] [4]It is suggested as the first line of treatment for early-stage Trypanosomabruceirhodesiense and second-line treatment for Trypanosomabruceigambiense. [4].

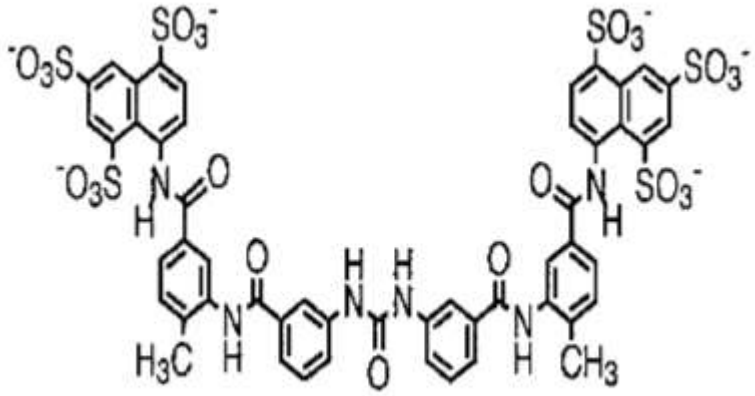
River blindness has been treated using it (onchocerciasis).reas of the world where the disease is prevalent (WHO). [5]

Suramin is given by injection into a vein

Suramin is a versatile chemical with a wide range of potential uses, including the treatment of cancer, autism, and a variety of viral and parasite illnesses. Suramin is another mysterious chemical.

Chemistry of suramin

It is a symmetric molecule with a functional group called urea (NH-CO-NH) in its centre. Suramin has four amide functional groups (in addition to the urea) and six sulfonic acid groups, as well as six aromatic systems, including four benzene rings sandwiched between two naphthalene moieties.



Suramine

molecular weight	1297 Da
H-bond donars	12
H-bond acceptors	23
LogP	0.00023
Protein bonding	99.7%

1.1 Mechanism of action:

Suramin's exact mode of action is unknown, however it is believed that parasites can selectively absorb the medicine when it is bound to low-density lipoproteins and, to a lesser extent, other serum proteins, through receptor-mediated endocytosis. [6]

1.2 Pharmacokinetics of suramin:

Suramin must be administered intravenously because it cannot be taken orally. Local tissue inflammation or necrosis may arise after intramuscular and subcutaneous administration[citation needed]. Suramin is about 99-98% protein bound in the serum and has a half-life of 41-78 days average of 50 days; however, the pharmacokinetics of suramin might vary greatly across individual patients. The distribution of suramin into cerebral spinal fluid is poor, and its concentration in tissues is also significantly lower than that in plasma. Suramin is only minimally metabolised, and the kidneys are used for around 80% of its elimination. [5].

2. Different activities of suramin

2.1.Suramin used as autism

A severe developmental disorder that affects a person's capacity for interaction and communication is called autism.

The neurological system is impacted by autism spectrum disorder, which also has an impact on the sufferer's general cognitive, emotional, social, and physical health

The University of California San Diego School of Medicine's Robert Naviaux, MD, PhD, professor of medicine, paediatrics, and pathology, and colleagues conducted a small, randomised clinical trial and discovered that a single intravenous dose of suramin produced a dramatic, though temporary, improvement of core symptoms of autism spectrum disorder (ASD). The primary signs and symptoms of ASD are not currently being treated with any medications.

More generally, the study results are consistent with the "cell danger response theory," The researchers would like to point out that suramin is not authorised for the treatment of autism. Suramin can be harmful if provided incorrectly by unskilled workers, at the incorrect dose and schedule, without thorough assessment of drug levels and toxicity monitoring, as is the case with many intravenous medications. To discover how to utilise low-dose suramin safely in autism and to identify drug-drug interactions and uncommon adverse effects that cannot currently be predicted, careful clinical trials will be required over a number of years at several locations. We strongly caution against the unlawfuuseof suramin

According to may 13,2020 article ASD (autism spectrum disorder) is a complex illness with numerous potential causes. We think that, at its most fundamental level, ASD is a multisystem biological response to environmental and genetic stressors. It is known as the cell danger response and causes an excessive release of ATP, the primary energy carrier. The regular operation of many different types of cells, including how neurons cooperate and communicate, is disrupted by excessive ATP signaling

2.2 suramin against cancer

Suramin, a polyanionic substance that was initially created as an antiparasitic, has lately started to be used in clinical studies to treat a number of human tumours that are resistant to current treatment approaches.

Suramin's capacity to bind and deactivate growth factor and enzyme systems necessary for cellular homeostasis and proliferation underlies this.

Suramin has been the subject of pilot trials in adrenocortical carcinoma, prostate cancer resistant to conventional hormone therapy, and nodular lymphomas.

In the 1940s, researchers conducted the first studies on suramin's effects on neoplasms in animals. Suramin treatment simultaneously administered to mice with lymphosarcoma resulted in noticeably smaller tumours [(10).] It was demonstrated in the 1970s that

In mice with engrafted Ehrlich cancer, suramin may increase the effects of cyclophosphamide and adriamycin [(11).] In the 1980s, patients with advanced adrenal and renal cancer underwent the first suramin clinical trial [(12).]

None of the patients experienced a complete remission, however over half of the patients displayed either modest or partial responses. Nonetheless, a number of following suramin clinical trials were conducted

Suramin was specifically evaluated against bladder cancer [(22).] non-small cell lung cancer [(21).] prostate cancer , and non-small cell lung cancer [(22)]

In a xenograft mouse model, suramin and taxol together decreased invasiveness and stopped metastases [(66).] Suramin'schemosensitizing actions on tumour cells may be explained in a variety of ways, such as by inhibiting fibroblast growth factors and angiogenesis or telomerase [(26).] [(25).]

2.3 Suramine used as antidote

Suramin is a competitive, reversible PTpase inhibit

oSuramin's ability to inhibit thrombin, phospholipase A2, and purinergicsignalling are three of the many biological processes it can block, all of which suggest its potential utility as a protective agent.

Several vipers have poisons that resemble thrombin[(29),] cunningly starting the coagulation cascade in blood from mammals.

Suramin was suggested as a treatment for snakebite because it inhibits both thrombin itself [(30),] as well as the thrombin-like proteases found in snake venom [(31).]

The enzyme phospholipases A2, which transforms phospholipids into lysophospholipids, is another frequent component of metazoan venom

suggesting that itcan act as an antidote. A certain degree of protection from venoms by suraminwasconfirmed in mouse models [(32-34).] The potential use of suramin as an antidote is attractive, given the high global burden of snakebites [(35)] and the current shortage of antivenom [(36).]

Suramin's ability to block P2 purinergic, G protein-coupled receptors [(37)] maycounteract the action of neurotoxins that trigger arachidonic acid signaling, e.g., viaphospholipase A2 activity [(38).]

A possible explanation is that suramin prevents theactivation of ATP receptors at the motor nerve ending, which otherwise would depressCa2 currents and reduce acetylcholine release at the presynaptic membrane [(39).]

2.4 Suramin used as antiviral agent

From the middle of the 20th century, suramin has been recognised to have antiviral and antibacteriophage properties [(42,43).]

Suramin was shown to inhibit retroviral reverse transcriptase shortly after retroviruses were discovered [(44),] which provided a justification to test Human immunodeficiency virus suramin (HIV).

Suramin reduced the viral burden in some of the research participants who had AIDS and protected T cells from HIV infection in vitro [(45),] but it had no effect on clinical symptoms or immunological characteristics [(46-48).]

Suramin was later discovered to bind to the HIV-1 envelope glycoprotein gp120 and prevent host cell attachment, indicating that the in vitro protection against HIV infection is mediated by inhibition of viral entrance [(49).]

Suramin also prevents the dengue virus from attaching to host cells by directly affecting the viral envelope protein [(50).]

Herpes simplex [51] and hepatitis C [52] viruses were also discovered to inhibit host cell attachment, which explained the Suramin has been shown to have protective effects against duck hepatitis B virus infections in vivo and in vitro [53] as well as herpes simplex virus infections [54].

Due to its inhibitory effect on the viral DNA polymerase, suramin had initially been tried against hepatitis viruses, much to the experience with HIV [55.56]. Suramin, however, was discovered to be harmful and ineffective in chronic active hepatitis B patients in a small clinical investigation [57].

Enterovirus 71 (EV71) was neutralised by suramin by attaching to capsid proteins in cell culture and a mouse model [58-60

It's been proven to inhibitWith the Chikungunya virus, both RNA synthesis and replication occur [61].

When present at the time of infection, suramin offered protection in vitro, and this was explained by a decrease in viral host cell binding and uptake [62

Table 1 Diseases and pathogens susceptile to suramine

Disease and/pathogens	cell culture	Animal model	Patient
parasitic infections	X	X	X
T.B.rhodesiense	X	X	X
surra,T.evansi	X	X	NA
River blindness,O.volvulus	X	X	X
T.cruzi	X		
Leishmania spp.	X		
P.falciparum	X		
viral infections			
hepatitis	X	X	X
AIDS	X		X
herpes simplex virus	X	X	
Chikungunya virus	X	X	
Enterovirus 71	X	X	
Dengue virus	X		
Zika virus	X		
Ebola virus	X		
Neoplastic disease			
Non-small cell lung cancer	X	X	
breast cancer	X	X	
bladder cancer	X	X	
brain tumors	X	X	
prostate cancer		X	X
other			
snake bite	X	X	
arthritis	X	X	
autism	NA	X	X

NA-not applicable x-activity

3.Precaution and warnings for suramin[63]

3.1 Warnings

This drug contains topical hydrocortisone, neomycin, and polymyxin. If you have an allergy to hydrocortisone, neomycin, polymyxin topical, or any other ingredient in Cortisporin Cream, do not use it.

3.2 Contraindication

hypersesitivity

3.3 caution

Proteinuria and renal toxicity reported with use

Avoid use in renal or hepatic impurity

5.Proper suramine usage

5.1 Dosing:

5.1.1 For injection dosage form:

For African sleeping sickness:

Adults and children—Dose is based on body weight and must be determined by your doctor.

5.1.2 For river blindness:

Adults—Dose is based on body weight and must be determined by your doctor.

Children—Use and dose must be determined by your doctor.

6. Adverse effect of suramin

A medication may have undesired side effects in addition to the ones that are required. Although though not all of these side effects are likely to occur, if they do, medical treatment may be required.

Cloudy urination, skin crawling or tingling, diarrhoea,

dizziness, especially after skipping meals

headache heightened irritation due to skin tone

itchiness, joint pain, and appetite loss

nausea

numbness or weakness in arms, hands, legs, or feet skin rash, sensation on skin\swelling on skin\stenderness of the palms and the soles\stire easily\svomiting

7. Conclusion

Suramin is still under debate. Is the company's poly pharmacology a strength or a weakness? Is it harmful or is it a shield? Timeless or out of date? There is hardly another molecule with as many biological actions as suramin, regardless of the judgement. The prospective targets are listed asoutstanding, and the flow of publications on Suramin is continuing. Most articles do not discuss trypanosomes or try panosomiasis. The list of probable targets should still be viewed with caution, however, because suramin's versatility in protein binding and negative charges can result in a variety of artefacts.

Suramin has the ability to dissolve Matrigel · which can produce a false-positive result in cell-based screening campaigns that employ Matrigel as support, such as those for angiogenesis inhibitors ·

Suramin, however, has a high affinity for albumin and may provide false-negative results in cell-based studies that use mammalian serum. Suramin has a variety of diverse drug-target interactions, nonetheless, notwithstanding the many confounders.

parasitology. However, molecules that act similarly to suramin may be identified viatarget-based screening once the mode of action is understood—new molecules thatare more specific and less toxic and possess better pharmacological properties than suramin

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