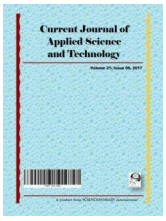

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Electrostatic Attraction: Inhibitory-mechanism of *The Medicinal Synthetic Aluminum-magnesium silicate* against Electrically Charged Disease-agents (*Human immune deficiency virus*/Cancer-cells/Other viruses/Infected cells) and the Medicine`s Adjuvant Effects –Review

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Authors' contributions

The authors collaborated for the review. Authors MCOE and MES conducted the literature search. Author MCOE drafted the manuscript . Authors IJO, EK and NUN processed the manuscript for publication. All the authors read and approved the final manuscript.

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ABSTRACT

Aim: To review mechanisms of actions of *The medicinal synthetic Aluminum-magnesium silicate* (MSAMS) as, antiviral, antiretroviral and anticancer medicine and as adjuvant.
Materials and Methods: Literature-review for information on Aluminum-magnesium silicate (AMS) as a pharmaceutical binder/stabilizing agent and results of experiments on effects of electrostatic attraction, between AMS-*Nanoparticles* and opposite electrical charges, on disease-agents.
Findings: AMS is traditionally a pharmaceutical binder for drug-formulations. It binds medicines

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because its molecular *Nanoparticles* have negatively charged surfaces and positively charged edges. Viruses and abnormal cells (cancer and infected) are also electrically charged. So, AMS bonds to the disease-agents by opposite-charges` electrostatic attractions. For that reason, it has antiviral and anticancer effects. As a silicate, it stimulates immunity. It is also a stabilizing agent. Stabilizing medicines prolongs bioavailability. Again, *Nanoparticles* deliver drugs to targets. Prolonging bioavailability and improving delivery enhance efficacy of antimicrobials. Enhancing efficacy leads to enough clearance of infections so that immunity completes their termination to prevent development of drug-resistance. Enhancing efficacy of antimicrobials also reduces their doses, needed to achieve desired effects, thus reducing side effects of drugs, to further enhance patients` immune responses. Synergy between enhanced efficacy of medicines and enhanced patients` immunity, leads to clearance of resistant secondary infections and termination of viral infections. By reducing doses of drugs, concentrations of their active ingredients in formulations are reduced thus minimizing their cost. AMS is not found in every county and even in countries where it is found, it contains impurities. So it requires purifying to make it safe. However, oxides and silicates of Aluminum and Magnesium are already approved medicines being used for treatments. So, Aluminum silicate was reacted with Magnesium silicate to get MSAMS: $Al_4(SiO_4)_3 + 3Mg_2SiO_4 \rightarrow 2Al_2Mg_3(SiO_4)_3$.

Conclusion: MSAMS mops HIV/other viruses and cancer-cells. It normalizes immunity and improves efficacy of medicines. Synergy between these MSAMS-effects and immunity inhibits electrically charged disease-agents.

Keywords: Electrostatic bonding to viruses/cancer-cells; enhancing immunity; clearing secondary infections (drug-resistant/sensitive).

1. SYNTHESIS OF MEDICINAL ALUMINUM-MAGNESIUM SILICATE

Aluminum-magnesium Silicate (AMS) occurs as natural mineral deposits in India and in the United States of America. It is an off-white or creamy white, odorless, tasteless, soft slippery small flakes or fine powder. It has a density of 2.41g/cm and a moisture content of 6.0 to 9.98% and is insoluble in water, alcohol and organic solvents. The compound is a polymeric complex of Aluminum, Magnesium, Silicon, Oxygen and Water. Its average chemical analysis is expressed as 13% Magnesium oxide, 61% Silicon oxide, 2% Calcium oxide, 0.1% Titanium oxide and 0.9% Feric oxide [1].

The complex is composed of three lattice layers of octahedral alumina and two tetrahedral silicate sheets. The Aluminum is often substituted to varying degrees by Magnesium, Potassium or Sodium to balance the electrical charges. Iron, Lithium, Calcium and Carbon could be present in smaller quantities. In the pharmaceutical industry, Aluminum-magnesium silicate is marketed as Veegum® or Pyropes®. Other synonyms for the pharmaceutical raw material include Aluminosilic acid, Carisob, Geisord, Magnabite, Magnesium-aluminum silicate.

Each molecule of the AMS is composed of submicroscopic platelets (0.96 nm thick). So, the molecules are made of *Nanoparticles*. *Nanoparticles* of AMS are staked in sandwich fashion with a layer of water between each. Faces of the *Nanoparticles* have negative electrical charges, while their edges are positively charged. The net negative electrical charge of the platelets is balanced by Sodium and other cations.

Aluminum–magnesium silicate is an adsorbent, a viscosity-enhancing agent, an anti-caking agent, a stabilizing agent, a tablet and capsule des-integrant and tablet binder. It is stable indefinitely when stored under dry conditions. It can function well both under high pH and low pH but is insoluble in water and other solvents. AMS is generally non toxic and nonirritating and so, has been used in drug formulations for many years. It is used in formulation of tablets, creams and ointments because of its properties as adsorbent, stabilizing agent, suspending agent, tablet and capsule des-integrant, viscosity increasing agent and tablet binder. It is used in oral and topical formulations and has been reported to be safe for use in systemic treatment of food animals. The AMS is a good binding agent because of the positive and negative electrical charges that coexist on its molecules.

However, the natural AMS contains lots of impurities [1] which could be injurious to animals or humans. It is usually treated, to reduce the

impurities by blending it with water to form slurry. This removes the impurities and separates out the colloidal fractions. The refined colloidal dispersion is then drum-dried to form small flakes which are micro-atomized to get the powder grade.

Two other minerals found in many countries including Nigeria, Aluminum silicate {$\mathbf{Al_4\ (SiO_4)}$} and Magnesium silicate ($\mathbf{Mg_2SiO_4}$)} have chemical structures similar to Aluminum-magnesium silicate and are already approved medicines for treatment of diseases in man and animals [2]. So, to synthesize medicinal grade of AMS, devoid of impurities, Aluminum silicate was reacted with Magnesium silicate [3] : $Al_4(SiO_4)_3 + 3Mg_2SiO_4 \rightarrow 2Al_2Mg_3(SiO_4)_3$. Dextrose monohydrate (simple sugar) was formulated with the MSAMS to convey the *Nanoparticles* across mucous membranes of the gastro-intestinal tract, into blood-circulation by active transport [4].

2. MSAMS: EFFECTIVE AGAINST IMMUNE DEFICIENCY VIRAL INFECTIONS

Small sizes of viruses allow them access to infect cells, inaccessible to most medicines [5]. So, antiviral medicines need complementation from immunity. HIV can be as small as 110 nm [6] and it destroys lymphocytes (cells responsible for general immunity). HBV and HCV [7] are even smaller (22-55 nm) and they impair the liver, organ central for innate and adaptive immune responses [8]. Because lymphocytes are not life-sustaining, their destruction does not lead to immediate death. So, HIV establishes chronic infections. The liver has great ability to regenerate. So, HBV and HCV also lead to chronic infections. For chronic nature of HIV/HBV/HCV-infections they require prolonged treatment**.** Prolonged medication with antiviral medicines of biochemical-effects causes toxicity (because of similarity between viral biochemistry and biochemistry of human cells). Medicines that work by physical effects (mopping/binding) must reach every infected cell before achieving complete cure. Infected cells that are inaccessible to antiviral-medicines are the cells called “sanctuary-cells “or “reservoirs of the infections”. By destroying lymphocytes and impairing the liver HIV/HBV/HCV-infections cause immune deficiency. Under the state of immune deficiency, physical-effect medicines which do not reach all infected cells cannot terminate viral infections.

Nanoparticles that form molecules of Aluminum-magnesium silicate have two electrically charged ends. One end has positive electrical charges while the other has negative electrical charges. Viruses also have electrical charges. The viral genome is made of a number of positively charged ions, such as, Na^+, Mg^{++}, K^{+++} while the phosphate component is negatively charged. So, the DNA viruses end up with net negative charges while the RNA viruses end up with net positive charges [5,7]. Therefore, the two classes of viruses have points of attachment on *Nanoparticles* of Aluminum-magnesium silicate.

Difficulty in developing antiviral drugs is due to similarity between biochemistry of viruses and biochemistry of animal cells. For that reason, substances which inhibit viral biochemistry also have some effects on biochemistry of human or animal cells. Attraction between electrical charges of the AMS-*Nanoparticles* and viruses is a physical effect and so does not have adverse effect on animal cells. Also, silicates are safe for use as medicines [9] and the *Medicinal synthetic AMS* is a formulation of two medicines that are already approved [2].

The AMS-*Nanoparticles* are only 0.96nm thick (smaller than: HIV, HBV, HCV). So, they reach all cells these viruses can reach. Since edges of the *Nanoparticles* are positively charged and their surfaces, negatively charged while HIV and HCV are positively charged and HBV negatively charged [5,7,10] AMS-*Nanoparticles* use their surfaces to mop HIV and HCV while they mop HBV with their edges. Abnormal cells are negatively charged [11]. Therefore, the *Nanoparticles* also bond onto infected cells with their edges and destroy them [1]. The "sanctuary cells" (infected cells) are also destroyed. So, "hidden infections" are unmasked. When all particles of a virus infecting patients` organs/tissues are mopped out, they are cured. Also, silicates are immune stimulants [12]. Added to these, AMS stabilizes antimicrobials [1]. Stabilizing medicines prolongs their bioavailability. Prolonging bioavailability improves efficacy of medicines [13]. With improved efficacy, lower doses of antimicrobials achieve desired effects and use of lower doses for treatments minimizes side effects of medicines. Minimizing side effects of medicines adds to enhancement of patients` immune responses. Synergy between Antiviral effects of the *MSAMS,* improvement in efficacies of antimicrobials and enhancement of patients` immune responses lead to better treatment of viral infections and

Table 1. CD4 counts and viral loads of HIV/AIDS patients currently on clinical trial of *The Medicinal synthetic Aluminum-magnesium silicate*

Months:	0		2		3	
Patients	**CD4**	**VL**	**CD4**	**VL**	**CD4**	**VL**
A	0	160,000	88	25,000	129	5,000
B	207	<20	359	<20	512	<20
C	115	<20	411	<20	500	<20
D	229	60,000	501	18,000	675	4,600
E	205	45,000	388	12,000	477	2,789

secondary infections so that even the immune deficiency diseases (HIV/AIDS, HBV- and HCV-infections) become curable[14].

In vitro, mean HIV titer of specimens treated with the MSAMS increased (P=0.009) from 4.00±1.60 to 14.00±2.00 suggesting that hidden HIV-infections were unmasked by the MSAMS-treatment. When the specimens-MSAMS treatment was repeated, the viral titer reduced (P=0.024) from 14.00±2.00 to 6.50±1.50 suggesting that the MSAMS mopped HIV from the specimens [15].

For *In vivo* trial of the MSAMS on HIV/AIDS patients the treatment is combined with antioxidants-treatment to prevent oxidative stress which could result from the HIV infection [16] and from HIV-infected cells being destroyed by positively charged ends of the MSAMS-*Nanoparticles.*

In one of the trials [17,18], HIV-viral loads of the patients reduced at rates of 86% in 4 weeks, 96% in 8 weeks and 99.71% in 12 weeks. In another trial [19,20], viral loads in 8 patients treated with the MSAMS increased (P=0.006) from 498.50±33.37 to 1,072.50±184.55 after 3.75±2.06 weeks before decreasing (P=0.04) to 407.33±297.27 after 6.67 weeks and from 24,250.00±15,939.34 to 321.00±229.38 (P=0.045) after 12.00 weeks. In a third trial [20, 21], mean-CD4 count of 10 patients reduced (P=0.008) from 496.80±194.39 to 263.90±149.26 after one month before increasing (P=0.001) monthly to: 507.90±133.19; 692.70±113.34; 840.20±139.41; 1007.30±163.50; 1537.10± 302.10; 1924.60±247.45; 2449.00±190.70; 2707.00±837.87 and 3034.00±153.48. Mean of their viral loads increased (P=0.020) from 1,820.30±868.75 to 2,855.90±960.98 after first month, before reducing (P=0.0.030) monthly to: 1,565.20±743.17; 759.20± 473.65; 345.50±115.01; 192.80±97.40; 95.00± 55.80; 37.40±26.46; 17.50±16.88; 14.33±3.65 and 0.00±0.00 (HIV infection terminated).

In an ongoing clinical trial, two patients who had been on antiretroviral therapy for a long time had their HIV-infections suppressed (viral loads less than 20) before the trial but their CD4 counts were still very low (207 and 115< 500). After three months of the MSAMS trial, their CD4 counts increased to 512 and 500 respectively (≥500). Restoring normal CD4 counts (immunity) is one of the mechanisms by which *The Medicinal synthetic Aluminum-magnesium silicate* terminates HIV-infections. Failure of existing ARVs to normalize CD4 counts may be reason they do not achieve permanent cure of HIV/AIDS.

Patients sick of *Hepatitis B virus* (negatively charged) tested negative to HBV surface antigen after two weeks of MSAMS-treatment while it took 20 weeks of treatment before a patient sick of HCV (positively charged) became antibody negative.

Other electrically charged disease-agents on which MSAMS has proved to have inhibitory effects include RNA viruses {positively charged: *Peste des Petits Ruminants Virus* (PPRV), *Measles virus* (MSV), *Newcastle disease virus* (NDV), *Infectious bursa disease virus* (IBDV) and *Avian Influenza virus* (AIV} and negatively charged disease-agents such as DNA viruses {*Eggdrop Syndrome virus* (EDSV), *Canine Parvovirus* (CPV), *Fowl pox virus* (FPV)} and abnormal cells (infected cells and cancer cells).

3. EFFECTS OF MSAMS ON OTHER POSITIVELY CHARGED DISEASE-AGENTS (RNA VIRUSES)

For effect of the MSAMS on *Peste des petits ruminants virus* (PPRV), though HA titers of samples of PPRV treated with the MSAMS did

not change from titers of the portions used as controls, the treatment significantly reduced sero-conversion ability of PPRV [23] from a mean HI titer of 9453.70±2418.30 to 64±14.49 ($P< 0.05$).

To test effects of the MSAMS on NDV [24], samples of Velogenic *Newcastle disease* virus were treated with the MSAMS. The treatment was repeated on the viral supernatants. For effect of the MSAMS on morbidity of NDV, three groups of chicks were challenged. In one group, each chick was infected, by intramuscular (I/m) route with a virulent NDV, treated with the MSAMS once. In the second group, each chick was infected with the same NDV after it was treated with MSAMS twice. In the control group, the chicks were similarly infected with same NDV sample without first treating it with the MSAMS. For effect of the MSAMS on mortality of NDV infected chicks, two groups, each of 20 chicks were used. One group was infected by injecting each chick with NDV, I/m. The second group was infected by introducing NDV-infected chicks into their pen. At onset of clinical signs of ND the two groups were each sub-grouped into two. One sub-group was treated with MSAMS in drinking water (2 g/liter), for seven days. The second sub-group served as control. Incubating NDV samples with the MSAMS *in vitro*, reduced the viral titer (HA) from 613±86 to 4.5±0.72 ($P< 0.05$). Also, incubating NDV with the MSAMS once reduced its morbidity rate from 100% to 20% while incubating the virus with the MSAMS twice reduced the morbidity from 100% to zero. When chicks were infected by I/m inoculation of NDV, both the group treated with MSAMS and the control, had 100% mortality each ($P>0.05$). However, when infection was by mimicking the natural mode of infection, treatment with the MSAMS reduced mortality from 20% to zero ($P< 0.05$).

Reduction in titer of NDV following incubation with the MSAMS and failure of portions of the virus incubated twice with the medicine, to reproduce ND in susceptible chicks infected by I/m inoculation, suggest that the MSAMS-*Nanoparticles* mopped out the virus. Also, in the control, clinical signs of ND were observed 40 hours post infection (P/I) but in the group inoculated with same NDV incubated with the MSAMS only once, even the two chicks that became sick, showed clinical signs of ND, 120 hours PI. This suggests that even the single incubation with the MSAMS reduced NDV-load of the samples drastically. The low morbidity (20%) and prolonged incubation period in the group inoculated with NDV incubated with the MSAMS only once, agrees with reduction in the viral titer, *in vitro*.

For effects of the MASMS on *Infectious bursa disease virus* (IBDV) both the virulent virus and the vaccine were tested [25]. QAGPT titer of IBDV sample treated with the MSAMS (*in vitro*) reduced from 8 to zero, while sero-conversion ability of the treated vaccine reduced from AGPT 13.60±1.22 to 0.00±0.00. Mortality of IBDV infected chicks treated with the MSAMS also reduced from 30% to zero. These reductions in titer of IBDV, in sero-conversion ability of IBD vaccine and in mortality of IBDV-infected chicks suggest that the MSAMS inhibited IBDV and its activities.

Volumes of *Avian Influenza virus* (AIV) samples treated, *In vitro*, with the MSAMS reduced at a mean rate of 23.4±5.48 % [26]. Also, incubation with the MSAMS significantly ($P=0.001$) reduced titer of the H_5N_1 AIV, from a mean HA, 73 ±32.72 to 1.4±0.43 and the EMR from 100 to 65%. Incubating AIV with the MSAMS increased MDT of chicken embryos inoculated with AIV significantly ($P=0.002$) from 76±4.38 to 128.00± 18.36 hours. Repeating incubation of AIV with the MSAMS reduced titers of the viral samples from HA, 128 to HA, 2 in both the portion incubated with MSAMS once and in the two portions incubated twice and thrice respectively. EMR of chicken embryos was 100% in the control and in the group inoculated with AIV portion treated with the MSAMS once, but their MDT increased from 64 hours in the control to 104 hours in the group inoculated with AIV portion treated with the MSAMS once. In the group of eggs inoculated with portions of the AIV treated with the MSAMS twice and thrice respectively, there was no embryonic death.

Reduction in volume of AIV samples suggests that the MSAMS adsorbed onto water molecules in the samples. This action of the MSAMS agrees with reported effect of natural AMS on water. Reduction in volume of viral samples should lead to increase in the viral titer, if the MSAMS had no effect on the virus. However, the viral titers reduced despite the reduction in volume. This suggests that electrostatic attraction between the MSAMS –*Nanoparticles* and the viral particles was stronger than the attraction between them and water molecules.

4. EFFECTS OF MSAMS ON OTHER NEGATIVELY CHARGED DISEASE-AGENTS (DNA VIRUSES AND INFECTED/CANCER CELLS)

HA titer of samples of *Eggdrop syndrome virus* (EDSV) treated with the **MSAMS** [27], *in vitro,* reduced (P<0.05) from 22.50±7.59 to 2.00±0.65. Also, sero-conversion ability of the viral portions treated with the medicine reduced (P<0.05) from a mean HI titer, 42.20±11.19 to 00.00±0.00.

Significant reduction of titer of EDSV in samples treated with the **MSAMS**, *in vitro,* suggests that the virus bonded to opposite charges on the MSAMS-*Nanoparticles* by electrostatic attraction. This will inhibit the viral replication process at the first stage. Reduction in number of viral particles, available to establish infections in cells of the challenged chicks may be responsible for the reduction in antibody titer of EDSV in the chicks. In infected chicks, viral particles released from infected cells would also adsorb onto the MSAMS-*Nanoparticles* so that number of new foci of infection would reduce. Reducing foci of infection would enable body immune system overcome viral infections, thus leading to cure.

Incubating samples of *Canine parvovirus* (CPV) with the MSAMS reduced their viral titer from 875.6±261.7 to 270.8±132.1 (P<0.05). All treated dogs (both adults and puppies) recovered while all the untreated dogs died [28]. Gross pathology of the untreated dogs revealed swollen heart with rounded apex, pale-swollen lungs and congested liver in the puppies. Untreated adult dogs had discolored and swollen intestines, congested and swollen liver and pale-swollen lungs on gross post mortem examination. Histopathology revealed necrosis and cellular infiltration of crypts of the duodenum, necrosis of hepatocytes, presence of pyknotic hepatocytes, dilation of the hepatic central veins and necrosis of the myocardial cells. There was no gross pathology in treated dogs except for pale lungs. Regenerating cells were also observed at histopathology of livers and duodenum of the treated dogs.

Reduction in CPV titers of the samples treated with the MSAMS agrees with results of incubating other viruses with the medicine. The viral particles may have adsorbed onto the MSAMS by electrostatic attraction and were removed from the samples, *in vitro*. AMS is un-absorbable, yet it was able to inhibit pathologic effects of CPV in the heart, lungs and liver. This finding suggests that Dextrose monohydrate (simple sugar) in the drug formulation was able to convey the charged molecules across mucous membranes of gastro-intestinal tract of the treated dogs, by active transport [4].

For effects of the MSAMS on Fowl pox virus (FPV) five batches of the vaccine were each reconstituted with PBS, at the rate of 5 ml for each 200 doses [29]. Four ml of each of the reconstituted vaccines were treated with equal volume (4 g) of *the **MSAMS*** and kept at room temperature for one hour. The mixtures were then centrifuged for 10 minutes, at 2000 revolutions per minute. The incubation with MSAMS was repeated by mixing a volume of supernatants of the vaccines (2 ml) with equal amount of the MSAMS (2 g). The mixtures were again incubated at room temperature and centrifuged. Modified passive haemagglutination test [30] was used to test the supernatants. The MSAMS significantly (P<0.05) increased viral titers of FPV in the vaccines from a mean of 2.80 ± 1.10 to 11. 20 ± 4.38 but when the treatment was repeated, viral titers of all the vaccine-batches reduced (P<0.05) to 0.00.

In replication cycle of *Fowlpox Virus*, after the viral materials have assembled, the new virions get released by two methods. Some virions bud off the host cells completely while others remain attached on cells` surfaces. Viruses that remain attached to host-cells would not be able to sensitize (infect) RBCs and so would not produce passive agglutination of the RBCs. So, their presence would not be detected by the test used.

AMS has been reported to assist in disintegrating capsules within gastrointestinal tracts of treated patients. It is therefore possible that the first incubation with the MSAMS led to disintegration of cells used to culture the *Fowlpox Virus* in the process of vaccine production. So, virions that were still attached to cells` surfaces were released. *Fowlpox Viruses*, released from the cells, may have sensitized the sheep RBCs at higher dilutions of the vaccine supernatants, thus leading to the significant increase in viral titers of the vaccines, from 2.8±1.10 to 11.8± 4.38. The observation that when samples of some viruses are incubated with the MSAMS, their titers increase instead of reducing was also made with HIV and PPRV [15,23].

Nanoparticles have been reported to have selective effects on abnormal cells. So, ability of the MSAMS to disintegrate FPV-infected cells to release associating virions suggests that it also

has effects on infected cells. This suggests that MSAMS is among *Nanoparticles* that have anticancer effects. Its affinity for infected cells would also aid its antiviral effect of unmasking "hidden infections".

Ability of *the Medicinal synthetic Aluminum-magnesium silicate* to disintegrate infected cells was further investigated by using it to treat cell cultured Measles vaccine, cell cultured Peste des Petits Ruminants vaccine and cell cultured Newcastle disease vaccine. Samples of Measles vaccine (cell cultured *Measles virus*), PPR vaccine (cell cultured *PPR virus*) and of a cell cultured Newcastle Disease vaccine were treated with equal amount of the MSAMS, on volume to weight basis (V/W) and kept at room temperature for one hour before they were each centrifuged at 3000 revolutions per minute for ten minutes. Supernatant of each of the virus samples was tested for viral titer. Counter immuno-electrophoresis (C.I.E) was in addition done for the PPR vaccine. Incubation with the MSAMS was repeated on each viral sample until its highest hemagglutination titer or C.I.E. reaction was obtained. Portions of each of the viral samples, not incubated with the MSAMS served as controls.

Cell cultured *Peste des Petits Ruminants virus*, cell cultured *Measles virus* and cell cultured *Newcastle disease virus* all tested negative by haemagglutination test but when they were incubated with the MSAMS they produced agglutination of the respective RBCs [31,32]. These results suggest that the MSAMS disintegrated infected cells in which the viruses were "hiding" so that they became extra-cellular to cause haemagglutination. *In vitro* studies with the MSAMS on HIV also showed initial increase in titers of treated viral samples before they decreased, suggesting that the medicine destroys abnormal cells to unmask intra-cellular viruses. HIV/AIDS patients treated with it also had reductions in their CD4 lymphocytes counts initially and subsequently, continuous increases in the CD4 counts which, again, suggests that infected CD4-lymphocytes (abnormal cells) were destroyed before cell regeneration led to the increases. Increase in viral titer of HIV-positive plasma treated with the MSAMS and the increases in viral loads of patients in their first month of treatment which was followed by reduction in CD4 counts also indicate that the MSAMS destroys virus infected cells.

Four cancer-patients (two of colon cancer, one of breast cancer and one a case of fibroid) currently on trial of the Antivirt® have the clinical manifestations either diminished or totally disappeared. The cancerous breasts have even reduced less than normal size.

When "hidden infections "are unmasked, there would no longer be places of safety (sanctuary) for infections. However, unmasking intracellular pathogens may reactivate arrested infections that are not sensitive to the MSAMS. This may be responsible for some diseases/symptoms often observed in some HIV/AIDS patients at start of the MSAMS treatment. Diseases so far confirmed, to associate with treating HIV/AIDS patients with the MSAMS include malaria, typhoid fever and renal insufficiency. While malaria and typhoid fever could be results of reactivation of arrested infections, renal insufficiency may be due to oxidative stress. Destruction of infected cells leads to release of free radicals. So patients undergoing the treatment should also be placed on antioxidants, to mop free radicals.

5. ANTIMICROBIALS-STABILIZING (POTENTIATING) EFFECTS OF THE MSAMS

Aluminum-magnesium silicate is a stabilizing agent for medicines. By stabilizing medicines, AMS protects them against rapid degradation (metabolism). It thus prolongs bioavailability of drugs which increases potency of antimicrobials [13] which means that doses needed to achieve desired effects will reduce. If doses required for desired effects are reduced, active principles of drugs in their formulations would also reduce and their costs of production would reduce. Formulating antimicrobials in AMS could make them effective for treatment of resistant infections. Ability of *the Medicinal synthetic Aluminum-magnesium silicate* to enhance potency of antimicrobials [33] has been tested on Ampicillin trihydrate against bacterial infections[34], Piparazine citrate against *Heligmosomoides bakeri* [35] infection, Chloroquine sulphate against *Plasmodium berghei* infection[36] and on Sulphadimidin against coccidian and resistant bacterial infections [37,38]. It has also been tested on Ampicillin trihydrate against an Ampicillin-resistant infection [39].

Clinical signs of coccidiosis observed in chicks, infected with *Eimeria tenella* and *E. maxima,* included wing drooping, anorexia, depression, ruffled feathers and bloody diarrhea. Post mortem lesions seen, included ballooning of the

small intestines, petechial haemorrhages on serosal surfaces of the intestines. The intestinal walls were thickened and their lumens filled with blood and tissue debris. By the end of first three days of treatment, all the clinical signs including bloody diarrhea ceased in a group treated with 2 g of the 20% sulphadimidin-MSAMS drug formulation per liter of drinking water. The clinical signs also ceased in a group treated with 1g of 100% sulphadimidin per liter of drinking water, from the first day of second round of treatment (after observing two days break in treatment). However, the clinical signs (bloody diarrhea) persisted in a group treated with 5g of the sulphadimidin – MSAMS drug formulation and in a group treated with 0.4 g of 100% sulphadimidin. The group treated with 5 g of the sulphadimidin–MSAMS drug formulation per liter of drinking water and the group treated with 0.4 g of 100% sulphadimidin per liter of drinking water had mortality of 3 (30%) each. The group treated with the MSAMS-Sulphadimidin drug formulation at rate of 2g per liter (0.4g of sulphadimidin per liter) and the group treated with normal dose of sulphadimidin (1 g of sulphadimidin per liter) had one mortality (10%) each. The untreated group had nine mortalities (90%). Parasitological assessment showed that the group treated with the 20% sulphadimidin in MSAMS at rate of 5 g per liter (1 g of sulphadimidin per liter) had the least oocysts count per gram of feces (13,000), followed by the group treated with the normal dose, 1g of 100% sulphadimidin per liter of drinking water (15,000). The group treated with 2g of the 20% sulphadimidin in MSAMS drug formulation per liter had oocysts count of 16,000 per gram of feces while the group treated with 0.4 g of 100% sulphadimidin per liter of drinking water, had the highest oocysts count per gram of feces (965,000). The only survivor in the untreated (control) group, had oocysts count of 52,500 per gram of feces.

Since 5 g of 20% sulphadimidin drug formulation contains same amount of sulphadimidin as 1 g of 100% sulphadimidin, it was expected that the group treated with 5 g of the MSAMS-sulphadimidin formulation and that treated with 100% sulphadimidin at rate of 1g per liter would give same results. Instead, persistence of bloody diarrhea in the group of MSAMS-sulphadimidin and the 30% mortality were significantly different from the results of the group of 100% sulphadimidin, where the bloody diarrhea ceased and only 10% mortality was recorded. However, the low oocyst count of 13,000 per gram of feces recorded in the group of MSAMS-sulphadimidin and the 15,000 per gram recorded in the group of 100% sulphadimidin were approximately same. This suggests that sulphadimidin, effectively treated coccidiosis in both groups.

In the group treated with 0.4 g of sulphadimidin stabilized in MSAMS per liter, clinical signs ceased after three days of treatment and mortality was only 10%, while the group treated with 0.4 g of sulphadimidin without stabilizing it in the MSAMS had a mortality of 30% and the clinical signs did not cease. That group also had the highest oocysts count per gram of feces. These results suggest that the 0.4 g per liter was ineffective in the group of 100% sulphadimidin while it was effective in the group of MSAMS-sulphadimidin formulation.

It was therefore concluded that incorporating the MSAMS in sulphadimidin potentiated its anticoccidial activity. The 5 g of the 20% Sulphadimidin in MSAMS formulation per liter of drinking water became overdose hence the high mortality and persistence of bloody diarrhea which is clinical sign of overdose of Sulphadimidin but with low oocyst count per gram of feces. Also, the 20% Sulphadimidin in the MSAMS drug formulation which is equivalent of 0.4 g of Sulphadimidin per liter, which was ineffective became effective with only 10% mortality, 16,000 oocysts per gram of feces and cessation of clinical signs.

In an experimental treatment of resistant infections with MSAMS-drug formulations, normal dose of Sulphadimidine (1 g/liter of drinking water) led to increase ($P<0.05$) of load of Sulphadimidin-resistant *E. coli* infection by 259%. When the drug was stabilized with the MSAMS, load of the resistant infection increased further ($P<0.05$) by 789.10%. Reducing the dose to 75% (0.75 g/liter) and stabilizing it with the MSAMS reduced load of the resistant infection significantly ($P<0.05$) by 84.34%.

Normal dose of Piparazine (110 mg/kg) led to only 82.94% reduction ($P<0.05$) of EPG of feces of *H. bakeri*-infected mice [34]. When the drug was stabilized with the MSAMS, the rate of reduction improved ($P<0.05$) to 92.04%. Reducing the dose to 75% of Piparazine`s recommended dose (82.5 mg/kg) and stabilizing it with the MSAMS improved rate of reduction of the EPG ($P<0.05$) to 96.82%.

Normal dose of Ampicillin (10 mg/kg) led to only 80.68% reduction ($P<0.05$) of CFU/ml of bile of

S. gallinarum-infected chicks. When the drug was stabilized with the MSAMS the reduction improved (P<0.05) to 86.36%. Reducing the dose to 75% of recommended dose of Ampicillin (7.5 mg/kg) and stabilizing it with the MSAMS improved rate of reduction of the infection load (P<0.05) to 97.84%.

Normal dose of Chloroquine (7 mg/kg) led to increase (P<0.05) of parasitaemia of Chloroquine-resistant *P. berghei* infection by 15.27%. When the drug was stabilized with the MSAMS, the 7 mg/kg dose led to death of 80% of treated mice. Reducing the dose to 5 mg/kg and stabilizing it with the MSAMS reduced (P<0.05) the parasitaemia by 56.38%.

Normal dose of Ampicillin (10 mg/kg) led to reduction (P<0.05) of load of Ampicillin-resistant *E. coli,* just by 50%. When the drug was stabilized with the MSAMS, rate of the drug-resistant infection reduction decreased (P<0.05) from 50% to 43.91%. Use of 75% of the normal dose (7.5 mg/kg) stabilized with the MSAMS plus immune stimulants in feed of the chicks led to reduction (P<0.05) of load of the resistant infection by 95.78%.

These results suggest that stabilizing antimicrobials with *the Medicinal synthetic Aluminum-magnesium silicate* improves rate of clearance of drug-sensitive infections but it worsens cases of drug-resistant infections. AMS is a stabilizing agent. It prolongs bioavailability of antimicrobials. Also, its molecules are made of *Nanoparticles* and *Nanoparticles* cross blood-brain barrier and enhance delivery of drugs to targets.

Prolonged bioavailability and enhanced delivery of drugs to targets, improve both their antimicrobial effects and their side effects. This may explain the relief got by treating drug sensitive infections with the MSAMS-drug formulations at recommended doses of the drugs while they made drug-resistant infections worse. Reducing doses of drugs should mean that their effects would reduce, but when doses of three of the drugs used in the experiments were reduced to 75% of their recommended doses, stabilizing them with the MSAMS achieved better infection clearance than their normal doses, so stabilized. That suggests that reducing doses of Piparazine, Ampicillin and Chloroquine may have minimized their side effects while actions of the MSAMS on the drugs (prolonging bioavailability and enhancing delivery to targets) may have enhanced antimicrobial effects of the lower doses.

When dose of Ampicillin was reduced to minimize its side effects and it was stabilized with the MSAMS, supporting the treatment with immune stimulants cleared 95.80% of an Ampicilline-resistant infection. The strategy of minimizing side effects of drugs by using 75% of their recommended doses, potentiating antimicrobial effects of the drugs with the MSAMS and enhancing immune responses of patients, lead to enough clearance (≥95%) of infections so that they do not develop resistance against drugs used for their treatment. It also leads to cure of drug resistant infections.

Apart from prevention and treatment of drug resistant infections, use of lower doses of drugs would reduce cost of treatments and also reduce amount of drug residues in human foods of animal origin (meat, milk and eggs). This would again reduce incidences of drug resistant infections in human beings who eat foods of animal origin.

6. CONCLUSION

MSAMS-*Nanoparticles* use electrostatic attraction between positive charges on their edges and the negative charges on abnormal cells to destroy infected cells and so unmask "hidden infections" (initial CD4 counts-reductions and viral loads-increases). They may also destroy cancer cells because cancer cells are negatively charged too. The MSAMS-antioxidants regimen also elicits proliferation of CD4s (496.80±194.39 to 3034.00±153.48). With such high CD4 counts, there may no longer be hiding places ("**Sanctuary cells**") for viral infections. HIV infection-loads` reduction-rates depend on CD4 counts. MSAMS-treated HIV/HBV/HCV patients become negative.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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