EAS Journal of Pharmacy and Pharmacology
Abbreviated Key Title: EAS J Pharm Pharmacol
ISSN 2663-0990 (Print) & 2663-6719 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-1 | Issue-2 | Mar-Apr-2019 |

Research Article

An Evaluation of Toxicological Studies of Colloidal Silver Life Water: An Alternative to Antibiotics?

Raphael Nyarkotey Obu, RND, PhD.

Nyarkotey College of Holistic Medicine Tema C7 Ghana.

*Corresponding Author
Raphael Nyarkotey Obu, RND, PhD. Email: oburalph30@yahoo.co.uk

Abstract: **Aim:** One of the most important quantitative outputs from toxicity studies is identification of the highest exposure level (dose or concentration) that does not cause treatment related effects that could be considered relevant to human health risk assessment. The aim of this research article is to examine the toxicity of colloidal silver life water manufactured by Edigaf Services as alternative to antibiotic. **Method:** Six (6) Samples of the said product was sent for analysis at Kwame Nkrumah University of Science and Technology (KNUST), Ashanti region, Ghana to the Departments of Pharmacology for toxicological analysis. Two tests were carried out. In the first test, twenty animals were divided into two groups, control (n=10) and test animals (n=10). The control received ad libitum of normal tap water while the test group was provided with Silver life water. Both groups were given normal rodent feed (Agricare Ltd, Kumasi, Ghana). Water bottles (300 ml) were refilled as and when needed. Animals were then observed daily for 5 days for signs of toxicity. In the second test, rats were divided in 3 groups (n=5) and treated with 0, 5 ml/kg and 8ml/kg of the test water (Silver life) and observed over 48 hours for signs of toxicity. **Result:** In the first test, none of the animals died during the study period. There were also no signs of toxicity attributable to the water under study. In the second test, none of the animals died during period and no signs of toxicity attributable to the test water treatment were observed. The lethal dose (LD50) of the water was estimated to be above 8 ml/kg. **Conclusion:** The results indicate that Silver life Water can be regarded as virtually non-toxic in rats when given ad libitum for 5 days. The LD50 is also estimated to be above 8 ml/kg body weight of rats.

Keywords: Homeopathic, Antibiotic, Colloidal silver, Silver Life Water, Raw Water.

INTRODUCTION:

The physicochemical properties of a drug govern its absorptive potential, but the properties of the dosage form (which partly depend on its design and manufacture) can largely determine drug bioavailability (purestcolloids.com/toxicity.php). This article addresses the toxicity studies of colloidal silver water.

Interestingly, the differences in bioavailability among formulations of a given drug can have clinical significance. Thus, the concept of equivalence among drug products is important in making clinical decisions. Chemical equivalence refers to drug products that contain the same compound in the same amount and that meet current official standards; however, inactive ingredients in drug products may differ. Bioequivalence refers to chemical equivalents that, when administered to the same person in the same dosage regimen, result in equivalent concentrations of drug in blood and tissues. Therapeutic equivalence refers to drug products that, when administered to the same person in the same dosage regimen, provide essentially the same therapeutic effect or toxicity. Bioequivalent products are expected to be therapeutically equivalent.

The same website (purestcolloids.com/ toxicity.php) article further continued that therapeutic problems (eg, toxicity, lack of efficacy) are encountered most frequently during long-term therapy when a patient who is stabilized on one formulation is given a nonequivalent substitute (as for digoxin or phenytoin). Sometimes therapeutic equivalence may be achieved despite differences in bioavailability. For example, the therapeutic index (ratio of the maximum tolerated dose to the minimum effective dose) of penicillin is so wide that moderate blood concentration differences due to bioavailability differences in penicillin products may not affect therapeutic efficacy or safety. In contrast,

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Journal homepage:
http://www.easpublisher.com/easjpp/

Article History
Received: 30.03.2019
Accepted: 15.04.2019
Published: 30.04.2019

bioavailability differences are important for a drug with a relatively narrow therapeutic index.

The company, Purest Colloids, Inc. hired one of the leading independent laboratories in the U.S. to do a toxicology study on our colloidal silver product, Mesosilver. The test, called an LD-50 test, was performed in accordance with the guidelines of the Federal Hazardous Substances Act (FHSA) Regulations, 16 CFR 1500. In the test work, the Mesosilver was given to a number of both male and female test animals. The amount of Mesosilver given to the animals was 5g/kg of 20 ppm colloid, or the equivalent of a 200-pound man taking 30 tablespoons at one time (the normal adult dosage is between one teaspoon and four tablespoons/day). As a result of the test work, the independent laboratory made the following conclusion, "Under the conditions of this study, there was no mortality or significant evidence of toxicity observed in the rats. The test article Mesosilver would not be considered toxic at a dose of 5g/kg by oral route in the rat." bioavailability - Extent to which--and sometimes rate at which--the active moiety (drug or metabolite) enters systemic circulation, thereby gaining access to the site of action.

The physiologic characteristics and comorbidities of the patient also affect bioavailability.

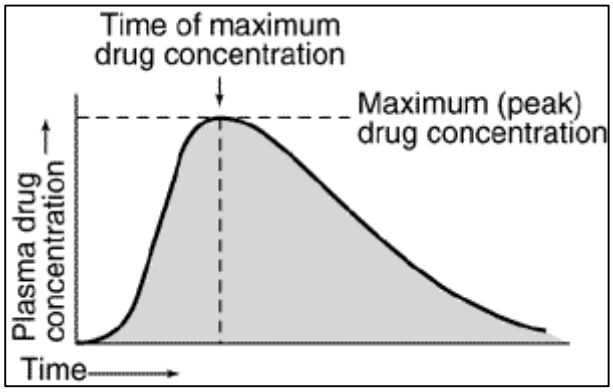


Fig.3. Source: purestcolloids.com/toxicity.php

Fig 3. Representative plasma concentration-time relationship after a single oral dose of a hypothetical drug. Area under the plasma concentration-time curve is indicated by shading.

The plasma drug concentration increases with the extent of absorption; the peak is reached when the drug elimination rate equals absorption rate. Bioavailability determinations based on the peak plasma concentration can be misleading, because drug elimination begins as soon as the drug enters the bloodstream. The most widely used general index of absorption rate is peak time; the slower the absorption, the later the peak time. However, peak time is often not a good statistical measure because it is a discrete value that depends on frequency of blood sampling and, in the case of relatively flat concentrations near the peak, on assay reproducibility.

Absorption rate is important because even when a drug is absorbed completely, it may be absorbed too slowly to produce a therapeutic blood level quickly enough or so rapidly that toxicity results from high drug concentrations after each dose. The plasma drug concentration increases with the extent of absorption; the peak is reached when the drug elimination rate equals absorption rate. Bioavailability determinations based on the peak plasma concentration can be misleading, because drug elimination begins as soon as the drug enters the bloodstream. The most widely used general index of absorption rate is peak time; the slower the absorption, the later the peak time. However, peak time is often not a good statistical measure because it is a discrete value that depends on frequency of blood sampling and, in the case of relatively flat concentrations near the peak, on assay reproducibility.

The most significant myth about silver is that it is neither safe nor effective for public consumption. The research on colloidal silver water safety is mixed with FDA issuing several warnings against products with silver. According to Gnat Ignatov and Oleg Mosin 2015, Silver (Ag) –is a metal with an atomic mass of 107.87 a.u.e. related to the sub-group of the first group of the periodic system of D.I. Mendeleev, has a pronounced physiological effect on the body, and is resistant to atmospheric oxygen at room temperature.

Hans Laroo 2013, also postulates that Colloidal silver consists of loose silver atoms forced by the tensions of the water to adhere into clusters in suspension. Accordingly, to refer to nano sized colloidal silver clusters as being metallic, is incorrect.

The heavy metal contents of colloidal silver has been a major subject of the toxicity studies. The big question is whether silver is a heavy metal, what is the right dosage and will product of such nature have a long term effect on humans? This current paper examines the physiochemical constituents of colloidal silver life water as homeopathic antibiotic and immune care in Ghana.

METHODOLOGY

Six (6)samples of the Colloidal Silver Water in an 750ml Brown Plastic Bottle were sent to the Kwame Nkrumah University of Science and Technology, KNUST, Ashanti region, Ghana to the Department of Pharmacology for toxicological analysis. This is in line with the FDA in Ghana requirement of product registration.

Two tests were carried out. In the first test, twenty animals were divided into two groups, control (n=10) and test animals (n=10). The control received ad libitum of normal tap water while the test group was provided with Silver life water. Both groups were given

normal rodent feed (Agricare Ltd, Kumasi, Ghana). Water bottles (300 ml) were refilled as and when needed. Animals were then observed daily for 5 days for signs of toxicity.

In the second test, rats were divided in 3 groups (n=5) and treated with 0, 5 ml/kg and 8ml/kg of the test water (Silver life) and observed over 48 hours for signs of toxicity.

DEPARTMENT OF PHARMACOLOGY
TOXICOLOGICAL REPORT

NAME OF SAMPLE: Silver Life
BATCH NO: 083662626

Table 1 Acute Toxicity

Animal Species	No. of animals/group	Route of administration	Doses administered	No. of death recorded	Duration of study
Sprague Dawley Rats	20 males, 2 groups (n=10)	Oral	*ad libitum*	No deaths recorded	5 days

Table 2 Acute Toxicity

Animal Species	No. of animals/group	Route of administration	Doses administered	No. of death recorded	Duration of study
Sprague Dawley Rats	15 males, 3 groups (n=5)	Oral	0, 5 ml/kg, 8 ml/kg	No deaths recorded	48 h

RESULT

In the first test, none of the animals died during the study period. There were also no signs of toxicity attributable to the water under study (Table 1).

In the second test, none of the animals died during period and no signs of toxicity attributable to the test water treatment were observed. The lethal dose (LD_{50}) of the water was estimated to be above 8 ml/kg (Table 2).

CONCLUSION

The results indicate that ***Silver life*** can be regarded as virtually non-toxic in rats when given *ad libitum* for 5 days. The LD_{50} is also estimated to be above 8 ml/kg body weight of rats.

DISCUSSION

According to one report (2019) Colloidal silver might seem like a promising option over antibiotics, but it still has some of the side effects of antibiotics. In another study (Maneewattanapinyo *et al*., 2011), the researchers conducted tests for acute oral toxicity, eye irritation, corrosion and dermal toxicity of colloidal silver nanoparticles (AgNPs) in laboratory animals following OECD guidelines. Oral administration of AgNPs at a limited dose of 5,000 mg/kg produced neither mortality nor acute toxic signs throughout the observation period. Percentage of body weight gain of the mice showed no significant difference between control and treatment groups. In the hematological analysis, there was no significant difference between mice treated with AgNPs and controls. Blood chemistry analysis also showed no differences in any of the parameter examined. There was neither any gross lesion nor histopathological change observed in various organs.

The results indicated that the LD50 of colloidal AgNPs is greater than 5,000 mg/kg body weight. In acute eye irritation and corrosion study, no mortality and toxic signs were observed when various doses of colloidal AgNPs were instilled in guinea pig eyes during 72 hr observation period. However, the instillation of AgNPsat 5,000 ppm produced transient eye irritation during early 24 hr observation time. No any gross abnormality was noted in the skins of the guinea pigs exposed to various doses of colloidal AgNPs. In addition, no significant AgNPs exposure relating to dermal tissue changes was observed microscopically. Their findings on toxicity tests in this study suggest that colloidal AgNPs could be relatively safe when administered to oral, eye and skin of the animal models for short periods of time.

A 2010 report by Alan B. G. Lansdown also proved that Silver allergy does occur but the extent of the problem is not known. A recent article 2018 to be accessed at https://sovereignsilver.com debunked the so many false report on toxicity of the silver water. In the said article, many peer reviewed literature papers in the field of toxicology end up with a PR department promoting sensational headlines claiming something is toxic. But toxicity depends upon the dose and route of administration.

A case study in the article is about water. For instance, drinking too much water (many gallons) at one time can lead to death. Inhaling a much smaller amount of water is commonly referred to as drowning. Yet we need drinking water to stay alive. A natural balance exists between our healthy bodies and nearly everything we encounter in the world around us. So how does one interpret the peer-reviewed literature that has sensationalized headlines like "Water Could Kill You"? In helping consumers make sense of this, the authors have taken the various units of silver exposure reported in the literature and converted them into what the equivalence to the EPA Daily Reference Dose would be.

The proper form of silver?

Another augment is centered on the right form of silver dose. Metals can be bound to different elements, which impacts their absorption and stability. A case study is, chromium VI, Erin Brockovich movie from many years ago, is an extremely toxic form of chromium and carcinogenic to humans. However, chromium in a different form such as polynicotinate is an essential, required nutrient employed by the body to enhance insulin action. This typically implies that one cannot say that all chromium is safe or toxic.

So unlike chromium, silver is not yet classified as an essential nutrient in the USA, however it does provide significant health benefits as proven in multiple research studies. The form of silver is important when considering safety. For example, silver nitrate (considered a silver salt) is used as an eye drop for newborns to prevent blindness, but it would be considered toxic to orally consume this form of silver.

Another typical case study is the Bio-active silver hydrosol (the form of colloidal silver in Sovereign Silver) that has been classified in Canada by the Natural & Non-Prescription Health Product Directorate (the risk assessment division of Health Canada, the Canadian equivalent to the US FDA) as a Trace Element, this therefore means that it is an essential element for the preservation of good health. It is a pure mixture of silver ions and silver nano-clusters in suspension, with the highest bioavailability of silver at >98%. The particles are smaller than any other form of silver, therefore it is very effective in the low, safe 10 ppm (parts per million) concentration.

This is similar to the Colloidal silver life Water produced by Edigalf in a safe dose of 10ppm(parts per million)concentration for used as homeopathic antibiotic in Ghana.

Colloidal Life Silver Water is also not based on nanotechnology which involves the measurements of the size of particles that are on the scale of nanometers. They could be engineered nanomaterials, such as electronics components in cell phones, or they could be naturally occurring nanomaterials, such as milk's protein colloids that give milk its white color and provide us with a healthy protein source.

While the particles are measured in nanometers, the product is not engineered nanotechnology, a defining characteristic of which is that particles are ENGINEERED at the nanoscale. Particles in Edigalf water are the result of silver's natural equilibrium state between ions and metal particles.

Edigalf Colloidal silver life water cannot be regarded as an engineered nanoparticle because:

• Nanomaterials have continuously existed in the food supply.

• Silver is a naturally-occurring element that is widely distributed, although at low concentrations, in drinking water and in food such as milk, wheat and mushrooms, and in the nanoscale. Peer reviewed literature provides evidence of naturally occurring silver colloids and silver nanoparticles in river waters in Texas (Wen *et al.*, 1997).

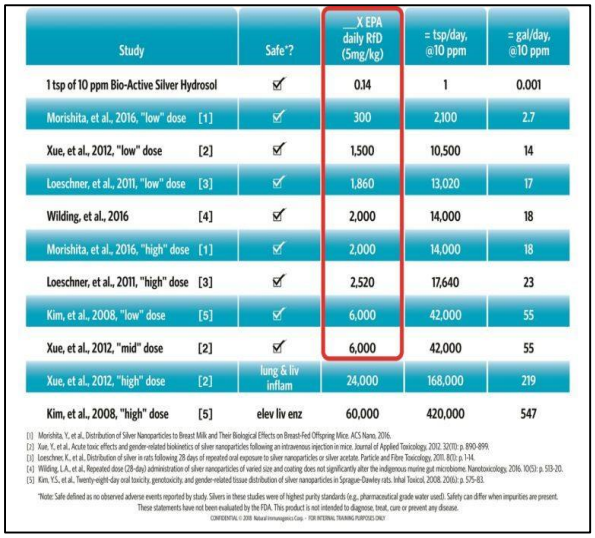
• Silver life water cannot be counted as an 'engineered nanomaterial' because the silver ions and nanoclusters are in a naturally occurring equilibrium balance due to the purity nature and the packaging in opaque glass to prevent light or oxygen from altering that natural balance.

• Colloidal silver has been consumed for over 120 years in different parts of the world, with a remarkable safety record. The few incidents of argyria have been associated with use of homemade silver-based products; abuse of such products with consumption many times the recommended dosage; the over-use of silver salts, silver proteins or compounds; or exposure via inhalation of silver dust.

Concentration	Tsp. once a day	Power dose 5-7 times daily
10 ppm	50 mcg	250-350 mcg
25 ppm	125 mcg	625-875 mcg
50 ppm	250 mcg	1,250-1,750 mcg
100 ppm	500 mcg	2,500-3,500 mcg
250 ppm	1,250 mcg	6,250-8,750 mcg
500 ppm	2,500 mcg	12,500-17,500 mcg
1,000 ppm	5,000 mcg	25,000-35,000 mcg
2,000 ppm	10,000 mcg	50,000-70,000 mcg

www.epa.gov — IRIS Report — Silver

Fig.1. Dosage form of silver: why colloidal silver life Water manufactured by Edigalf falls in the "safe grade". Colloidal Silver Life Water produced by Edigalf is made of 10ppm of silver. The Green zone represents safety and the Red zone represents danger.



Study		Safe*?	___X EPA daily RfD (5mg/kg)	= tsp/day, @10 ppm	= gal/day, @10 ppm
1 tsp of 10 ppm Bio-Active Silver Hydrosol		☑	0.14	1	0.001
Morishita, et al., 2016, "low" dose	[1]	☑	300	2,100	2.7
Xue, et al., 2012, "low" dose	[2]	☑	1,500	10,500	14
Loeschner, et al., 2011, "low" dose	[3]	☑	1,860	13,020	17
Wilding, et al., 2016	[4]	☑	2,000	14,000	18
Morishita, et al., 2016, "high" dose	[1]	☑	2,000	14,000	18
Loeschner, et al., 2011, "high" dose	[3]	☑	2,520	17,640	23
Kim, et al., 2008, "low" dose	[5]	☑	6,000	42,000	55
Xue, et al., 2012, "mid" dose	[2]	☑	6,000	42,000	55
Xue, et al., 2012, "high" dose	[2]	lung & liv inflam	24,000	168,000	219
Kim, et al., 2008, "high" dose	[5]	elev liv enz	60,000	420,000	547

(1) Morishita, Y, et al., Distribution of Silver Nanoparticles to Breast Milk and Their Biological Effects on Breast-Fed Offspring Mice. ACS Nano. 2016.
(2) Xue, Y., et al., Acute toxic effects and gender-related biokinetics of silver nanoparticles following an intravenous injection in mice. Journal of Applied Toxicology. 2012. 32(11): p. 890-899.
(3) Loeschner, K., et al., Distribution of silver in rats following 28 days of repeated oral exposure to silver nanoparticles or silver acetate. Particle and Fibre Toxicology. 2011. 8(1): p.1-14.
(4) Wilding, L.A., et al. Repeated dose (28-day) administration of silver nanoparticles of varied size and coating does not significantly alter the indigenous murine gut microbiome. Nanotoxicology. 2016. 10(5): p. 513-20.
(5) Kim, Y.S., et al., Twenty-eight-day oral toxicity, genotoxicity, and gender-related tissue distribution of silver nanoparticles in Sprague-Dawley rats. Inhal Toxicol. 2008. 20(6): p. 575-83.

*Note: Safe defined as no observed adverse events reported by study. Silvers in these studies were of highest purity standards (e.g., pharmaceutical grade water used). Safety can differ when impurities are present.
These statements have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.

Fig.2. A case study of the Bio-active silver hydrosol (the form of colloidal silver in Sovereign Silver) that has been classified in Canada by the Natural & Non-Prescription Health Product Directorate (the risk assessment division of Health Canada, the Canadian equivalent to the US FDA) as a Trace Element, this therefore means that it is an essential element for the preservation of good health. It is a pure mixture of silver ions and silver nano-clusters in suspension, with the highest bioavailability of silver at >98%. The particles are smaller than any other form of silver, therefore it is very effective in the low, safe 10 ppm (parts per million) concentration. With this assessment, the Ghana version of colloidal silver life water is thus within the effective low dose of 10ppm used for the animal analysis at the Department of Pharmacology at the KwameNkrumah University of Science and Technology, KNUST, Ashanti region, Ghana-West Africa.

CONCLUSION

Based on the toxicological report and literature view, the author of this research paper therefore recommends Colloidal Silver Water by Edigalf with concentration of 10ppm which falls within the safe grade of the EPA to be taken 2teaspoonful(10ml) three times (3x) daily which gives a power dose of 300mcg less than the 350mcg by the report. The colloidal silver life water in Ghana is also in the same region of the Bio-active silver hydrosol (the form of colloidal silver in Sovereign Silver) that has been classified in Canada by the Natural & Non-Prescription Health Product Directorate (the risk assessment division of Health Canada, the Canadian equivalent to the US FDA and Ghana FDA) as a Trace Element, this therefore means that it is an essential element for the preservation of good health.

Conflict of Interest

The author of this paper reports no conflict of interest

Acknowledgement

The author thanks his staff, Mr. George Nartey and student, Mr. Edward Gameli Fenuku for producing the Silver Life Water for the research.

REFERENCE

1. Ignatov, I., & Mosin, O. (2015). Studying the Properties of Microdispersed Colloid Silver Nanoparticles. *Journal of Medicine, Physiology and Biophysics*, *10*, 18-28.
2. Laroo, H. (2013). Colloidal nano silver-its production method, properties, standards and its bio-efficacy as an inorganic antibiotic. *J Phys Chem Biophys*, *3*(5), 100130.
3. Safety and Toxicity of Colloidal Silver · Sovereign Silver To be accessed at https://sovereignsilver.com › Silver101
4. Wen, L. S., Santschi, P. H., Gill, G. A., Paternostro, C. L., & Lehman, R. D. (1997). Colloidal and particulate silver in river and estuarine waters of Texas. *Environmental science & technology*, *31*(3), 723-731.
5. Is Colloidal Silver Healthy & Safe or Just Hype? | Wellness Mama. https://wellnessmama.com › Blog › Health Mar 25, 2019 –
6. Maneewattanapinyo, P., Banlunara, W., Thammacharoen, C., Ekgasit, S., & Kaewamatawong, T. (2011). An evaluation of acute toxicity of colloidal silver nanoparticles. *Journal of Veterinary Medical Science*, 1106220557-1106220557.
7. Lansdown, A. B. (2010). A pharmacological and toxicological profile of silver as an antimicrobial agent in medical devices. *Advances in pharmacological sciences*, *2010*.
8. Colloidal Silver Toxicity Study | Purest Colloids. Availablehttps://www.purestcolloids.com/toxicity.php.