SPIONs Weapons by Moringa Oleifera finally improves outcome of Multi-Organ Damages (MODs) Prevention: Fact or hype for Reason behind Fighting High Sepsis Rates

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Abstract—

Introduction: *Spinel ferrite nanoparticles (Superparamagnetic Iron Oxide Nanoparticles/SPIONs) semiconductors have been broadly reported to kill bacteria outside the human body. SPIONs as photocatalytic agents in coloring dye water treatment have different mechanisms, it's a redox reaction. SPIONs as MRI agents have the same principle as bacteria killer, to emit electromagnetic waves. Winning against the high prevalence of MODs and sepsis is the aim of this study.*

Method: *Review article of Ex/Em SPIONs semiconductor in Photothermal Therapy (PTT).*

Result: *Table of 16 references which support SPIONs as New Generation (NG) antibiotic to kill resistant bacteria inside the body.*

Discussion: *Moringa oleifera gold composite NPs vs. NG beta-lactams. SPIONs green synthesis gold composite NPs are used as photothermal therapy (PTT) based on inducing hyperthermia to kill bacteria inside the body: NG MDR eradication.*

Conclusion: *PTT therapy achieved with SPIONs, under NIR, is used to kill MDR, XDR, TDR micro-bacteria, fungi and cancer cells inside the human body.*

Keywords— Splenectomy, Moringa oleifera, Ferrite NPs, Antimicrobia resistant, Inside the body, PTT.

I. INTRODUCTION

Multi organ damages (MODs) is the terminal cases of sepsis. MODs is the highest incidence of all cause of death. Sepsis due to antibiotic resistance is almost the cause of death in all ICU hospital department nowadays. In this 3 decades, new antibiotic continuously found, but could not eradicate the Multi Drugs Resistance (MDR) bacteria inside the body. The using of super paramagnetic iron oxide nanoparticles (SPIONs) which induce hyperthermia to kill bacteria has been reported.[1] The using of Ferrite nanoparticles (FNPs) through green synthesis will eradicate all Microbe resistance: MDR, XDR, TDR, inside the human body where body tissue is most transparent to NIR. Shielding by skin melanin, UV kill all resistance bacteria only outside the human body. This study wants to reveal SPIONs green synthesis[2] e.g. from Moringa oleifera gold composite NPs used as photothermal therapy (PTT), based on inducing hyperthermia, to kill bacteria inside the body. The New/Next Generation (NG) MDR eradication, after the racing of new generation antibiotics era, is based on it. Excitation/Emission (Ex/Em) SPIONs semiconductors vs. Photocatalytic agents in coloring/dye water treatment[2,3] mechanism has been recorded. The mechanism of

SPIONs as MRI agent[4] VS. SPIONs AuF based on hyperthermia[1] to kill bacteria,[5] fungi,[6,7] cancer cells,[8] are the same with SPIONs for NG MDR/XDR/TDR antibiotics bacteria inside the human body.[1,5]

II. METHOD

Case report and review on hybrid my library recommendation of Google Scholar, ChatGPT, and academic search engine ScienceDirect, and EBSCOHost MEDLINE with Full Text. Inclusive and exclusive using keywords ITP/AML/MDS laboratory with Bayesian network and Review article using academic search engine My Library, ScienceDirect, and EbscoHost with Bayesian analytical and network of photothermal and hyperthermia induce by SPIONs (Superparamagnetic Iron Oxide Nanoparticles) in association with antimicrobia. Green synthesis was preferable.

III. RESULTS

The mechanism of SPIONs to kill bacteria, fungi, cancer cells has been reported outside and inside human bodies. Kind of spinel ferrite, size, specification, and kind reaction support the argumentation. Source of the semiconductors excitation and emission (Ex/Em) were recorded. The results are focus on SPIONs green synthesis, which have the safety and economic values. The result is on Table 1, is based on these mechanisms:

Antibacterial activities of spinel ferrite nanoparticles (SPIONs) have been reported.[1,5,9,10,11,12, 13,14,15,16,17]

The tests that used to measure the antibacterial properties of zinc ferrite, was 80%, respectively successful. Nanoparticle made of zinc ferrite had a strong antibacterial effect, also the copper ferrite.[18]

Hyperthermia in specific cell with semiconductors which adsorp only Infra Red/Radio Magnetic Resonance,[4,5,19] and do emission of Terahertz T-Ray/Mw.[1,5,9] Whereas Visible/UV light could not be adsorp into the human body cause fail to penetrate the skin melanin shielding.[19]

Emission of hyperthermia could only be in microwaves 1000nm (1mm) – 10 cm (10^{10} Hz-10^{6} Hz). Radiowaves is with lambda more than 10 cm. The frequency of visible light is 4 x 10^{14} Hz till 7 x 10^{14} Hz. Electromagnetic (EM) long wavelength more than 1m or 10^{6} Hz, become a radio wave which is used by TV and radio transmitter, differentiated by the size of the semiconductors. One terahertz is 10^{12} or 1000GHz. Wavelengths of radiation in the terahertz band correspondingly range from 1mm-0.1 mm (100 μm, micrometer). This 1 mm- 100 mm wavelength range tremendously high frequency with frequency range 0.3 THz-3 THz. Terahertz (THz) radiation occupies a middle ground where the ranges of microwaves and infra-red (IR) light waves overlap, known as the 'terahertz gap'. It is called a 'gap' because the technology for its generation and modulation of EM waves in this frequency range ceases to be possible by the conventional electronic devices used to generate radio waves and microwaves, requiring the development of new devices and techniques, including FIR (Far Infra-Red) Ex/Em, the semiconductor SPIONs to make hyperthermia in specific cell to kill cancer cells, and to eradicate MDR/XDR/TDR microbacteria in the body.

Terahertz radiation – also known as submillimeter radiation, terahertz waves, tremendously high frequency, T-rays, T-waves, T-light, T-lux or THz -consists of EM waves within the International Telecomunication Union/ ITU-designated. Milimeter-micrometer-nanometer-pico-femto-atto-zepto-yoctometer is the 7 metric prefixes, and 1 TeraHz is 1000 Giga Hz, then Mega Hz, Kilo Hz etc. Deci Hz = 0.1 Hz, nano Hz = 0.000 000 001 Hz. It is telling the frequency. Whereas <3000 GHz is in ITU designed. Visual wave length: 400-700nm ($7x10^{14}$Hz – $4x10^{14}$Hz). Feel the frequency in ITU with NIR 215-$400x10^{12}$Hz, Microwaves 10^{8}Hz, Radio waves 10^{4}Hz, whereas 1 GHz=10^{9}Hz, and 1000Gz =10^{12}Hz. Photothermal therapeutic (PTT) applications using SPIONs AuFerrite (AuF) based on hyperthermia to kill cells.[1,19]

Photocatalytic for coloring water treatment is on oxidation-reduction reaction is completely different from mechanism of Ex/Em semiconductor SPIONs.

This study is focus on hyperthermia by Ex/Em, but still reported the reported antibiotic based on redox reaction[10,12,] In the second column of table 1, the kind of SPIONs are recorded.

TABLE 1
SIXTEENS INORGANIC NANOPARTICLES (NPS) TO FIGHT FUNGAL AND BACTERIA INFECTIONS IN THE ANTIMICROBIAL RESISTANT ERA: SEMICONDUCTOR BASED

Study, year	Inorganic NPs	Fungal or bacteria	MDR/XDR/TDR/pts status	Source of Excitation
[1]Kharey, 2022	AuF Green synthesis	All Biomedical therapeutic and imaging	MRI, hyperthermia, PTT	~800-1100 nm
[9]Tylor, 2012	SPIONs	AB-resistant biofilm	Multiple bacterial functions	In magnetic field
[5]Billici, 2020	NIR SPIONs	Broad Spectrum antibacteria	PDT	NIR eradication
[10]Rajivgandhi, 2022	Zn and Ni dope CoFNPs	Efficient biofilm eradication	Preparation	Damage of extra polymorphic substances
[11]Rahmayeni, 2021.	ZnF SNPs	Photocatalysis and antibacterial application	Green synthesis	Hydrothermal method
[12]Malik, 2022	NiFe2O4	Anticancer, antibiotic activity	Green synthesis	Oxidative stress
[13]Omelyanchik, 2020	Green Co-Zn SF NPs	Intrinsic Antimicrobial Properties	Green synthesis	Magnetic
[14]Subbiahdoss, 2012	FNPs	Antibacterial agents gentamycin-resistance staphylococci	Hyperthermia SPIONs	Magnetic targeting of surface-modified
[15]Kombaiah, 2017	FNPs	Antimicrobial properties	Green synthesis	Optical Magnetic
[6]Kumar, 2021	Carrageenan NPs	Fungicide by thermal behavior	Biopolymeric Chitosan-Carrageenan nanocomposites 66-231 nm	Soil and water pollution
[7]Madkhali, 2023	Metallic NPs e.g. AuNPs Zinc oxide etc. CnT	Potent Antifungal Rx/ to combat human fungal diseases incl. Candida, Aspergillus	Invasive fungal infections mortality and morbidity	Disturb mitochondrial calcium homeostasis
[8]Niemirowick, 2017	Magnetic NPs	Antifungal Anti cancer agents	Induce Hyperthermia	Enhance photosensitizing processes
[20]Hosseini, 2018	beyond Neutron source and gamma-ray	Deep seated tumor	PDT	X-ray induce photodynamic therapy (PDT)
[16]Hu, 2023	Photo sensitizers	Antimicrobacterial	APDT can kill drug-resistant strains, fungi, and viruses	Photo sensitizers with light activation
[17]Dove, 2023	AgNPs	Antibiotic-resistant bacteria	Reduced the minimum inhibitory levels of aminoglycoside	
[19]Liu, 2023	AgNPs	Kill cancer and bacteria cells directly	PTT	Adsorp 800 nm (NIR) laser for heat generation

The PTT making hyperthermia to kill the cells[1,19] but many outside killing reported as redox reaction, the making of Reactive Oxygen Species (ROS) that kill the bacteria, the resistant bacteria.

IV. DISCUSSION

Various nanoparticles have designed and made with the aim to kill cancer cell and bacterial cell. Ferrites, a kind of ferrimagnetic ceramic with the formula of spinel ferrite MFe2O4 (M is bivalent metal ion, like Zn, Cu, Ni, Co, Fe, and Mn) are recognized

for their great chemical stability, electrical resistance, has magnetic and physical characteristic. As a semiconductor, spinel ferrite has unique qualities like thermal and chemical stability and the dependency of magnetic characteristics on particle size in offering in hyperthermal technical applications. Made by green methods has reported to kill bacteria, incl. antibiotic resistance microbacteria (similar size as mitochondria). With the hyperthermal technical applications, these MDR, XDR, TDR antibacterial where the terminal case of multi-organ damage (MODs) in sepsis, should have been cured on sepsis and pre-sepsis cases. In the human body, the Excitation (Ex) should be with IR, and outside the body could be by UV natural from sun light or from UV lamp. As semiconductors, each size will emit certain electromagnetic wave, needs in T-ray range (hyperthermia), which will kill the bacteria. It is like a semiconductor that use by a radio or television principle. How to insert the semiconductors in the bacteria will be in another articles, but could be like insertion of MRI agent using SPIONs[1,4] with the Excitation being radio-wave with magnetic resonance. Nowadays these biological and industrial green synthesis of SPIONs for MRI agents,[4] and killing cells inside the body are in economic value in INDUSTRY 4.0.

This study focusses on green synthesis extracted form leaves, but the other method of synthesis preparation sol-gel processing, citrate decomposition, wet-milling method, solid-state reaction, hydrothermal crystalline, coprecipitation, and polymer matrix precipitation, were also used to create the spinal ferrites. The supporting mechanism of killing microbacteria are as followed:

1. Cobalt ferrite,[4] Cooper ferrite,[18] Zinc ferrite,[7,11] Nickel ferrite[10] Excitation, by UV (superficial) not IR (through inside the body), depends on the source of excitation, the emission of hyperthermia (T-ray) depends on the size of the Ferrite Nanoparticles (FNPs). Photocatalytic size,[11,21] is bigger than size for the hyperthermia emission.[1] For both, uses[11] has been reported. Killing by Photothermal Therapy (PTT) inducing hyperthermia[1,17] under NIR irradiation.[1,5,19]
2. Inserting the semiconductor/SPIONs-MRI agent e.g. for the treatment of antibiotic-resistant biofilm, and GMF-Antibiotic Marker Genes,[9,24] which is used in the making of superior seeds.[24]
3. Photothermal Therapy (PTT)[1,9,19] is different to PDT for killing cancer cell.[12,22] The mechanism of PTT is also different than cancer diagnosis, target drug delivery, and treatment, which are no need of the making of hyperthermia.
4. Photo Dynamic Therapy (PDT) to kill, not to taken MRI image,[4] and MRI of infection and inflammation.
5. Bacteria (similar size as mitochondria), are killed in hyperthermal technical applications in antibiotic resistance microbacteria using NPs. Green Synthesis of AuNPs is used to kill.[1]

   Researchers are always looking for new PDT drugs, and new ways to give therapy. So do the New Drugs SPIONs/ FNPs to kill MDR/TDR/XDR micro-bacterial inside the body and cancer cells. A new PTT drugs that can target tumor cells better, can leave normal cells more quickly, and allow the treatment light to penetrate better, not only in agarose gel Petry dish.

   AuNPs from Pimenta dioica aqueous leaf extract for PTT.[1] And Cobalt doped and MgF SNPs From Moringa Oleifera,[3] later could be doped to another FNPs e.g. Zn and Ni for efficient biofilm eradication (antibiotic resistance).[10]
6. Beta lactams antibiotics killing beta-lactamase bacteria, and beta-lactamase inhibitors[23].

   Before this hyperthermia SPIONs for killing micro bacteria, beta-lactams and beta-lactamase inhibitors are conquering antibiotic pharmaceutical industry.

The single antibacterial weapons most prescribed antibiotic class and the top important in terms of sales is the beta-lactams, but still failed in the sepsis and pre-sepsis stage. It could years after beta-lactamases, in and out the hospital, and the last stage are MODs and Steven Johnson syndrome, an immune-complex-mediated hypersensitivity. Four main classes of beta-lactam antimicrobials are in clinical use, which consist of three types of bicyclic structure: the penicillin, the cephalosporins, the carbapenems, and monobactams. Each class are originally a natural product. Each has since undergone semi-synthetic derivatives. Ampicillin and methicillin are an extended antibacterial activity of penicillin i.e., Gram-negative bacteria (ampicillin), and to counter resistant strains of Staphylococcus aureus (methicillin).[23] Penicillins are contraindicated in patients with history of anaphylactic reactions or serious skin reactions, for example, Stevens-Johnson syndrome and toxic epidermal necrosis.

4.1 The beta-lactam resistance:

There are Class A, C, D, and metallo-beta-lactamases (MBLs; class B).[23] Divers class of this enzymes produced by bacteria that inactivating the beta-lactam antibiotic. Mobile genetic elements (MGE) e.g. GMO with antibiotic resistance marker genes (ARMGs). encoded in RNAi or on chromosomes.[24] These RNAi are inserted in superior seed to silence the non-demand

characteristic quality of form, color, size, etc. to be change to better wish. ARMGs is used to separate the successful inserted from the failed, because ARMGs is coupled with the part of the wishes inserted gene, and kanamycin ARMGs has been reported.[24] Extended-spectrum beta-lactamases (ESBL) which are produced by Gram-negative bacteria also needs to be covered by SPIONs PTT, whereas Carbapenems are one of the few remaining antibiotics that can treat ESBL-producing germs, but resistance enzymes that destroy these antibiotics are on the rise, too. Medicolegal trained all doctors incl. veterinarian to have indication to give antibiotics, and not giving for prevention, but it fail to provide for plants.[24] Methicillin resistant staphylococcus aureus (MRSA) is resistant to all beta-lactam antibiotics and many commonly used antibiotic groups. Multidrug-resistant (MDR) TB are resistant to at least isoniazid and rifampin, the two most potent TB drugs. XDR-TB is a rare type of MDR TB that is resistant to isoniazid, rifampin, a fluoroquinolone, and second-line injectable e.g. Kanamycin. Total drug-resistant TB (TDR-TB) is resistant to a wider range of drugs than strains classified as extensively drug-resistant TB.

4.2 The beta-lactamase Inhibitors (BLI):

The BLI represent the major strategy for combating b-lactamase-mediated resistance. Clavulanic acid as an irreversible inhibitor of the most widely distributed class A enzymes. Penicillin-inhibitor combinations have found wide application as treatments for healthcare-associated infections by beta-lactamase-producing organism (the resistance one). The BLI is now necessary better treatment options for beta-lactamase-producing microorganism NG.[23]

4.3 MDR to multi-organ damage (MODs):

The new application of new antibiotic drug discovery is pressed by antimicrobial new resistance now with the high prevalence of MODs as terminal cases of sepsis. Prevention of MODs as the cause of dead in almost hospital ICU due to sepsis, has to change the focus on hyperthermia mechanism to kill the microbial resistant. This review study is the first SPIONs green synthesis to kill microbial resistant inside the body incl. killing Betalactamases and betalactamase inhibitors.[23] The SPIONs semiconductors kill by inducing hyperthermia,[1,9] under NIR irradiation.[5,19] Their heating performance came from wavelength range of ~800-1100 nm which is a tissue-transparent NIR region.[1]

Using inorganic NPs to fight fungal infections in the antimicrobial resistant era,[25] and the effect of decorating SPIONs with Ag NPs on their Magneto-Photo Thermal Heating Efficacy,[1,7,19] become the solution of all MDR, XDR, TDR microbacteria in this sepsis-MDO era.[14,16,17,19] The SPIONs gold composite for MRI contras agent, hyperthermia, and photothermal therapy (PTT) application has been reported.[1,19]

V. LIMITATION

Removal of antibiotic in an antibiotic manufacture sewage similar mechanism to photocatalytic process in coloring dye (e.g. methylene blue) as photodegradation on organic pollutans, has a different principle with antimicroba.[1,16,17,19] In this study we limit the photodegradation, and focus on hyperthermia principle on antimicroba. Then this study do not discuss how ARMGs to make superior seed using RNAi[24] but focus on killing MDR/TDR/XDR, the beta-lactamase-producing organism (the resistance one) using SPIONs crystals.[9]

The using of SPIONs for the treatment of Antibiotic-Resistant Biofilms using SPIONs.[9,10,14]

SPIONs as MRI agent,[1,4] or as drug carriers (vector), are also limited, and focus as MRI agent of infection and inflammation, and hyperthermia to antibacteria.

The Photocatalytic and Antibacterial Activity Cobalt Ferrite from plant extract,[1,5,13,15] Magnetic and Intrinsic Antimicrobial Properties,[13] and other SPIONs activity non PTT are not specific included in this study.

The author also limits to the other green synthesis SPIONs similar to moringa oleifera, such as aloe vera, Psidium guajava tea, sea grass, etc. The limitation of SPIONs in Moringa oleifera has specify the basic principle mechanism on PTT to eradicate resistant microbacteria inside the human body in low cost.

Aqueous extract Moringa oleifera leaves (CuNPs) has antifungal activity, Carrageenan Nanoparticles against Phytopathogenic Fungi,[6] metallic nanoparticles as antifungal therapies non PTT to combat human fungal diseases.[7] Magnetic NPs candidacidal activity,[8] and killing cancer cells[8,12,19] are also limited.

Broad Spectrum antibacteria by PDT achieved with SPIONS under NIR irradiation were reported,[5] and also in PTT applications.[1,9,16,17,19] A PDT were also used in cancer cell therapy achieved with SPIONs,[8,12,16,19] mix PTT with Radiotherapy,[20]

and disturb metabolism enhance the efficacy of aminoglycosides against antibiotic-resistant bacteria,[17] and oxidative stress[12] has been limited.

This is the first review study reveal PTT achieved with SPIONs, excitation by NIR using to kill MDR, XDR, TDR, and other resistant microbial inside the body, to fight sepsis and MODs as early as possible. The using of SPIONs to fight fungal in the antimicrobial resistant era has also been reported.[25]

VI. CONCLUSION

SPIONs green synthesis gold composite NPs are used as NIR photothermal therapy based on inducing hyperthermia to kill bacteria inside the body: NG MDR bacteria eradication, prevent MODs in sepsis.

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CONFLICT OF INTEREST

Nothing financial interest

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