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ANTICANCER ACTIVITY OF SULFONAMIDES CONTAINING HETEROCYCLE COMPOUND SYNTHESIZED BY GREEN CHEMISTRY VIA SILVER NANOPARTICLES (GREEN NANOPARTICLES)- A COMPREHENSIVE REVIEW

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Abstract

In green chemistry, formulation of nanoparticles are using different natural sources such as plants, bacteria, micro-organisms, fungi, algae, etc. and synthesis of sulphonamides drugs using different conditions and sources such as under neat conditions, in an aqueous medium, PEG-400, green solvents, etc for the synthesis of sulphonamide and their derivatives. The synergistic effects of silver nanoparticles and sulphonamide derivatives in anti-cancer activity present a promising approach for improving cancer treatment outcomes. Their combined action offers advantages such as enhanced anticancer efficacy, reduced drug resistance, and minimized side effects. The combination of silver nanoparticles and sulfonamide drugs holds significant potential for improving anticancer therapies. Further investigations are required to optimize their dosages, explore suitable drug delivery systems, and evaluate their efficacy against different types of cancers. Additionally, understanding their mechanisms of action, investigating their interaction with tumour microenvironments, and exploring potential synergies with other anticancer agents will be vital for future advancements. However, further research is necessary to fully elucidate their optimal usage, evaluate their safety profiles, and translate these findings into effective clinical applications.

Key Words: *Green chemistry, Silver nanoparticles, Sulphonamide, Anti-cancer activity.*

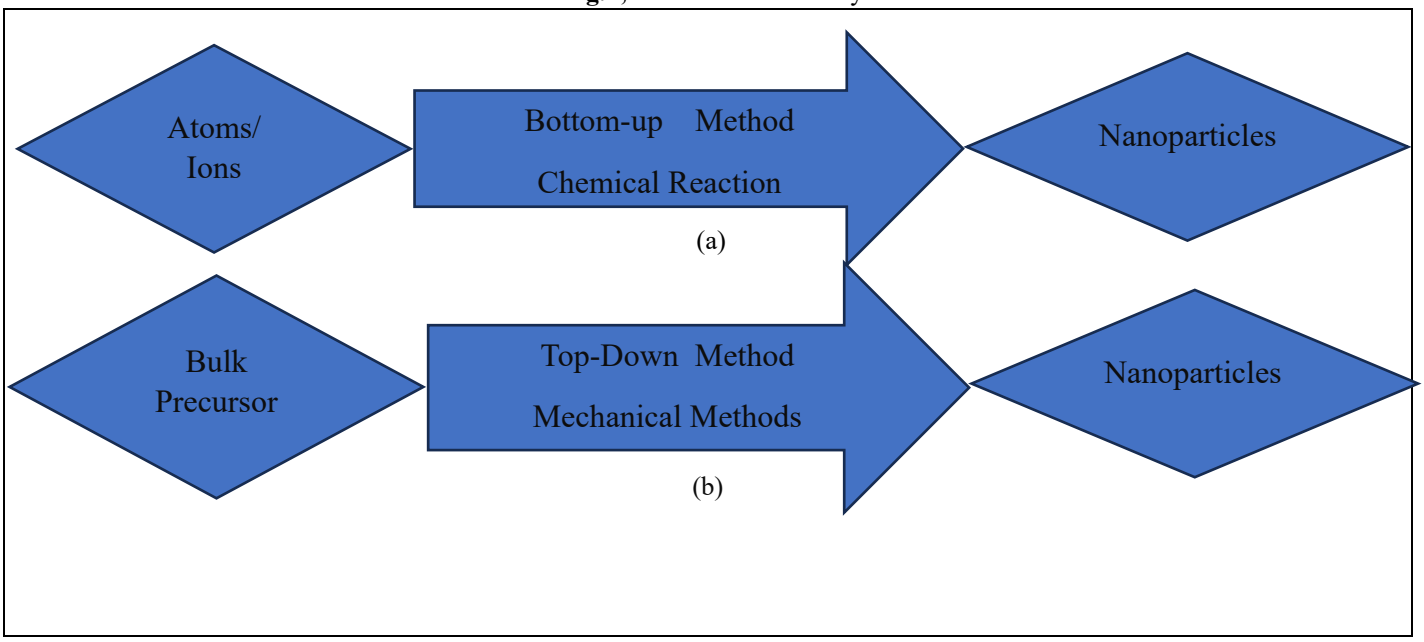
Introduction

In the exploration region, "green chemistry" is comprised of the union of synthetic mixtures and lessens or dispenses with the use/production of dangerous mixtures. The blend, use, and extreme removal of a compound item are undeniably covered by green science. Manageable science is characterized as compound designing in a way that is practical, innocuous, and non-harming and consumes the least measures of fixings and energy while delivering slight or no waste material so it is called "Green Science". That consoles plan of items and cycles that limit the utilization and age of unsafe fixings to HR and living life forms and regular assets for example decline contamination at its source. There are financially savvy and harmless to the ecosystem advances that increment item creation and lessen squander costs contrasted with biochemical methodologies. The field of "green science" centres around the utilization of substance techniques and approaches that reduce the utilization of unrefined components or side-effects from a compound response, solvents, impetuses, and so on,

in assembling, which produce dangerous materials that are hurtful to the climate or represent a gamble to human wellbeing. [1] Many people believe that green synthesis is a crucial device for reducing the adverse effects of traditional nanosphere synthesis techniques used in laboratories and enterprises. However, other aspects of chemically produced nanomaterials, such as dimensions circulation, shape, exterior charge, exterior chemistry, covering agents, etc., may occasionally have an impact on biological activities. Metal nanoparticles are used in a wide variety of productions, including radiation, gene therapy, pharmacology, and diagnostic tests. [2] These miniscule particles are known as nanosphere, and they are typically created using one of two techniques:

Methods include
(i) Top-down
(ii) bottom-up.
In contrast to the bottom-up method, which emphasizes organic and biotic methods, the top-down method places more emphasis on the physical way of nanoparticle creation. The pulsed laser decomposition, arc discharge, aerosol method, tumbling milling, vapour and gas phase, pulsed wire discharge, planographic printmaking process, etc. are all part of the physical synthesis approach. The creation of nanoparticles by a chemical interaction between atoms, ions, and molecules is referred to as the "bottom-up method" (fig. 1a). While the “top-down method” refers to using mechanical means to break up or crush large objects intoseveral parts to form nanoparticles. (fig.1b) [3]

Fig.1; Methods of Green Synthesis



Increasingly, nanoparticles are utilized in catalysis to speed up chemical processes. Its primary use is in catalytic converters for automobiles. Reducing the need for energy and raw materials, aids in the advancement of chemical synthesis. It is not a brand-new procedure. A highly useful and significant platform for delivering pharmacological substances more precisely to the targeted tissue and lowering doses and possibly hazardous side effects is the nanoformulation of medicines. Nanoparticles are a key element in the rapidly expanding area of nanotechnology because they exhibit special qualities as a result of their size, dispersion, and form. As a result of its success in enhancing the drug's pharmacokinetic profile, nanotechnology has garnered more attention. To get lower medication dosages, this entails improving the drug's solubility, dissolution rate, stability, and drug permeability. One of the primary objectives of employing nanoformulations is to improve therapeutic drug penetration through natural barriers, such as the blood-brain barrier (BBB). [4] The nanomaterials can be introduced directly to the target (especially intracellular pathogens), thereby enhancing drug/molecule bioavailability and stability as well as controlling its release, enhancing its activity, and/or avoiding its degradation and decreasing its toxicity. [5] In nanotechnology, the synthesis of nanoparticles like metal ions like silver, copper, gold, magnesium, and zinc that are synthesized by various methodologies using various sources like bacterial, fungal, plant resources, and algae under the condition that green chemistry is advantageous and prevents hazardous substances. Green nanotechnology proposes to synthesis of nanocomponents that don't affect the environment or human beings, as well as create nanoproducts that solve environmental issues.

In addition, there are numerous ways to make green nanoparticles, including
(a) phyto routes that use natural resources and their extracts, like plant’s root, stem, fruit, rhizomes etc.
(b) microbial routes that use bacteria, fungi, yeasts (eukaryotes), actinomycetes, and
(c) bio-template routes that use membranes, viruses, and diatoms as models.

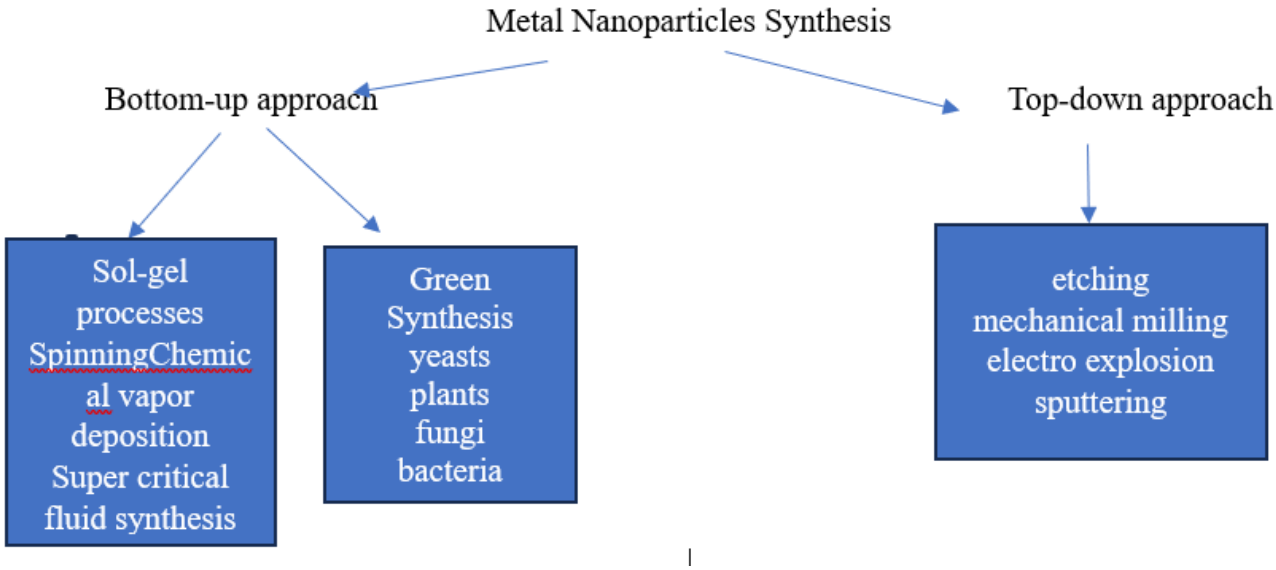


Fig.2; Metal Nanoparticle Synthesis

The presently set up tableware nanoparticles have important features for good conduction, chemical stability; reduced toxin;[6] and marvellous rectifier capabilities like anti-inflammatory; antifungal; anti-angiogenesis; antiplatelet; [7] antimicrobial exertion; [8] anticancer exertion; [9] and bactericidal exertion. [10] tableware participates in the normal manufacturing of nanoparticles in its nitrate form, which has a strong antibacterial effect. still, when tableware nanoparticles (AgNPs) are employed, the face area exposed to colourful microbe types rises noticeably. AgNPs are a pivotal element of nanotechnology since they do not alter live cells and can't, thus, lead to microbial resistance. Other uses for AgNPs include anticancer, particularly in this study, where they're employed both as effective & prospective motes on their own as well as an attacking targeted medicine delivery system for cancer discovery or webbing. AgNPs parade efficacy against a variety of cancer cells, including" Dalton's carcinoma" as cites excrescences, colon cancer" HT- 29 cells," cervical cancer" He La cells," and bone cancer" MCF- 7 cells".[6]

As preliminarily reported the conflation of AgNPs is prepared by natural sources like shops, fruit excerpt, etc. through green conflation. Natural sources contain colourful medicinal parcels with smaller side goods, lower toxicity, no adverse effects, and no chemical consumption. Green Nanoparticles are used for the development of chemotherapeutic agents having no side effects because AgNPs help in the junking of cell division by the pathway of cell death medium performing in cancer cell damage act as the anticancer effect of green nanoparticles against the MCF- 7 cell line.[11] Several studies have reported that the conflation of AgNPs under green chemistry is performed by natural sources like "*Momordica charantia"* fruit excerpt- intermediated AgNPs, which belongs to the Cucurbitaceae family prevents cell division through apoptotic pathway performed in damage of cancerous cell and act against MCF- 7 cell line.[11]AgNPs synthesized using synergistic waterless excerpts of the rhizome of "*Zingiber officinale*" and "*Curcuma longa*" were used for assaying *in-vitro* anti-cancer exertion against mortal colon melanoma '(HT- 29) cells '.[12]

Polyphenol curcumin is an enthusiastic substance component fundamental for pharmacological effort of "C. longa", it has strong anticancer packages against liver, pancreatic, colon, cervical, lung, cerebrum, endlessly bone malignant growths. What's more "*Zingiber .officinale*", for the most part called Ginger contain Asgingerols, zingerone, shogaols, parasols, and gingerdiols phytochemical fixings it's widely utilized as a cell reinforcement, mitigating, antihyperglycemic, immunomodulatory, hostile to malignant growth, and cardioprotective bundles. and further more generate DNA harm and chromosomal anomalies at low consideration without poison, particularly with no genotoxicity merchandise on human cells. [12] "*Senna alexandrina* Factory"(Leguminosae) utilizing the waterless passage of leaves-intermediated AgNPs is set up in the wild in Saudi Arabia, Yemen, and Egypt, and it's likewise significantly filled in Pakistan. flatware nanoparticles have been utilized in conventional medication to treat cholera, liver circumstances, clogging, typhoid, and different warm gestures. To address the traps of microbial protection from anti-toxins and dangerous circumstances, this work planned to create bioactive Ag-NPs (antibacterial and anticancer specialists) utilizing biosynthesis styles against mortal bone malignant growth cells (MCF-7). [7] "N, N, N-trimethyl chitosan chloride"(TMC) intermediated AgNPs (TMC/Ag) in one pot green conflation, is previously announced for inhibitory effort against cellular breakdown in the lungs. This nanocomposite utilizing as both a decreasing and calming specialist. Chitosan is a characteristic edge and settling specialist for clinical malignant growth treatment. [8]

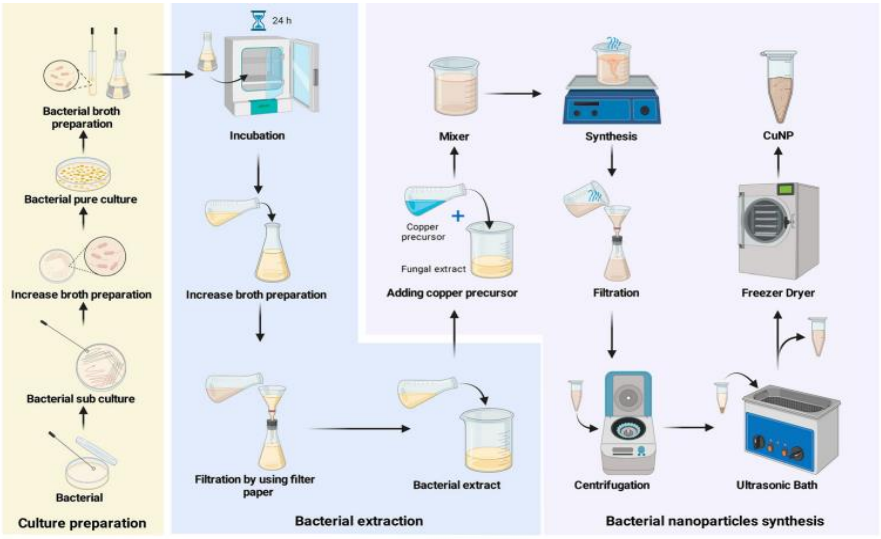


Fig.3; Diagrammatically presentation of synthesis of nanoparticles under green chemistry

The synthesized nanoparticles under green chemistry are significant for the synthesis of heterocyclic composites with an active scaffold of chemistry. Heterocycles are cyclic compounds found in organic chemistry that contain heteroatoms in the form of rings or cycles. Examples of heterocycles include those with C, N, S, and O arranged cyclically. The majority of heterocycles have unique features and several uses in medicine, fine chemicals, and the synthesis of novel pharmaceuticals. The different classes of heterocyclic compounds with nitrogen-containing have various pharmacologic and biotic applications like antiviral; antibacterial; antifungal; anticancer; and antimalarial. [13] However, sulfa drugs as sulphonamide derivatives are non-steroidal anti-inflammatory drugs. It is a significant group of compounds in both synthetic and medicinal chemistry. The sulfonamide also already has the structural concept of various drugs and bioactive compounds enriched with antibacterial; antitumor; anti-inflammatory; hypoglycemic; antipsychotic; anticancer; and protease inhibitor activity. [14] Different heterocyclic composites have been shown to limit the proliferation of nasty mortal cell lines when sulfonamide motifs are added. A(quinoxaline-2-yl) benzene sulfonamide outgrowth with strong anti-cancer action against the mortal liver cancer cell line(Hep G2) was created several new sulfonamide halves attached to quinoxaline pulpits, and their inhibitory goods against "VEGFR- 2"(vascular endothelial growth factor) were physiologically assessed. also, compound II showed excellent anti-cancer goods against the 'Hep-G2', 'HCT-116', and 'MCF-7' cell lines, with corresponding 'IC50' values of24.5 uM, 12 uM, and10.23 uM, whereas compound III presented 'IC50' values of22.9 uM,21.9 uM, and22.9 uM. [15]

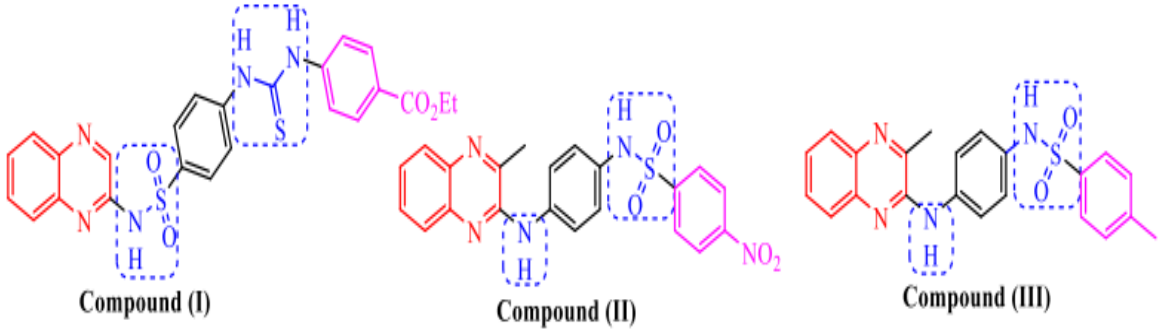


Fig.4; Structure of New Compounds of Sulpha Drugs

Vasculogenesis, embryogenesis, and angiogenesis are each regulated by the vascular endothelial growth factor and receptor, or 'VEGFR'. Three physically similar receptors, 'VEGFR- 1';' VEGFR- 2'; and 'VEGFR- 3' intervene in the natural exertion of 'VEGF'. A tyrosine kinase subtype called 'VEGFR- 2', which may intervene in microvascular permeability, proliferation, and isolation, is the main controller of 'VEGFR- 2'driven responses in endothelial cells. For the development of brand-new chemotherapy medicines, 'VEGFR-2' has been observed as an excellent clinical target'. In former paper bandy that the sulfonamide bearing different types of heterocycle composites designed a medicine to act as more potent anticancer agents, which are synthesized under green chemistry with using of lower dangerous chemicals and play a part as antiangiogenic exertion of 'VEGFR- 2' impediments. [15] Recently, expressed that few composites have been checked as strong hindrances of 'VEGFR-2' in-vitro or held antiangiogenic effort and satisfied clinical outcome in the therapy of malignant growth. Because of the significant piece of 'VEGFR-2' in angiogenesis, this receptor is the most imperative objective in enemy of angiogenic cures against malignant growth. A few strong 'VEGFR-2' obstructions have been created and endorsed for the therapy of bright diseasesd eg. 'Pazopanib (IV)'; 'sunitinib (V)'; and 'Sorafenib (VI)'.

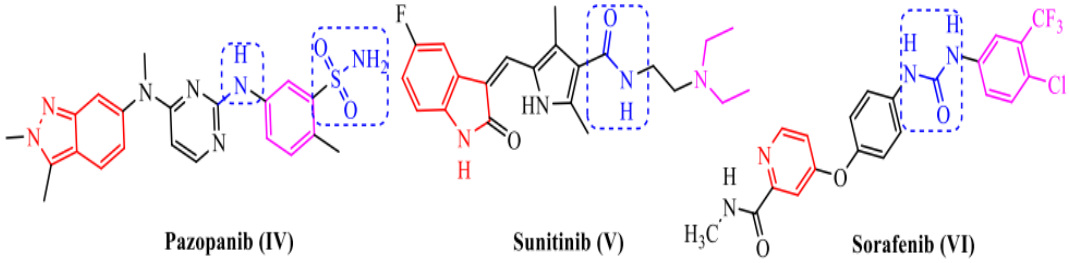


Fig 5

Ring extension and bioisosteric adjustment techniques for the VEGFR-2 inhibitors sorafenib and pazopanib were utilized to make the essential core of these particles at four unmistakable spots. By and large, three human growth cell lines — HCT-116, MCF-7 bosom disease, and HCC type HepG2 — were utilized as focuses for the proposed mixtures' in vitro antiproliferativeproperties.[15]

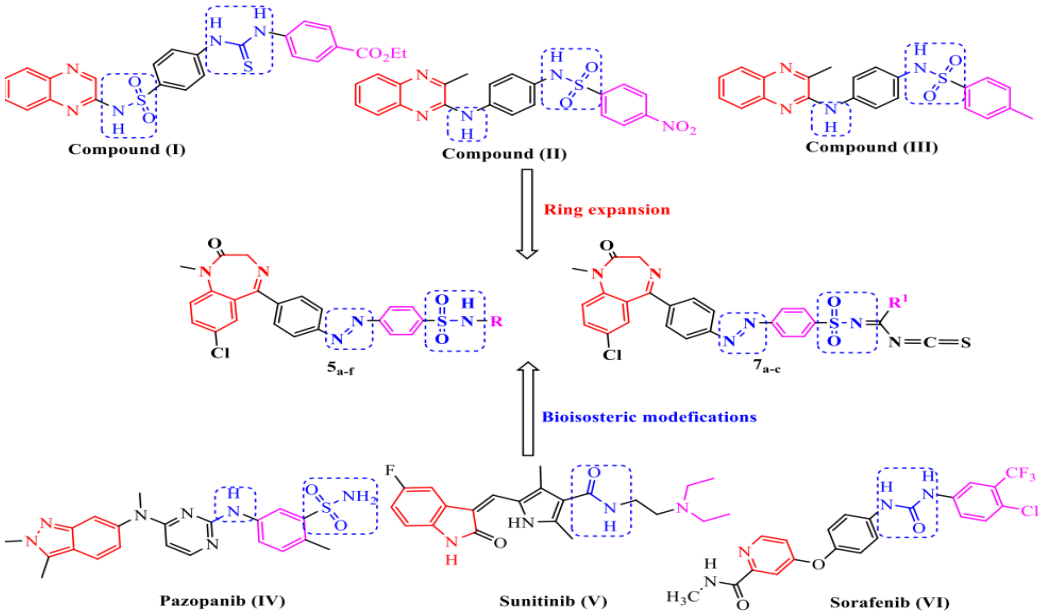


Fig.6; Derived VEGFR-2 inhibitors and our derivatives

Due to its strong biological activity, the introduction of the sulfonamide group with certain other heterocyclic rings, such as oxazolidinone, phthalimide, and quinolone, may be highly fascinating. Additionally, this combination may be found in benzothiazole skeletons like Ethoxzolomide, a sulfonamide medication that acts as a diuretic, and antitubercular compounds. [16]

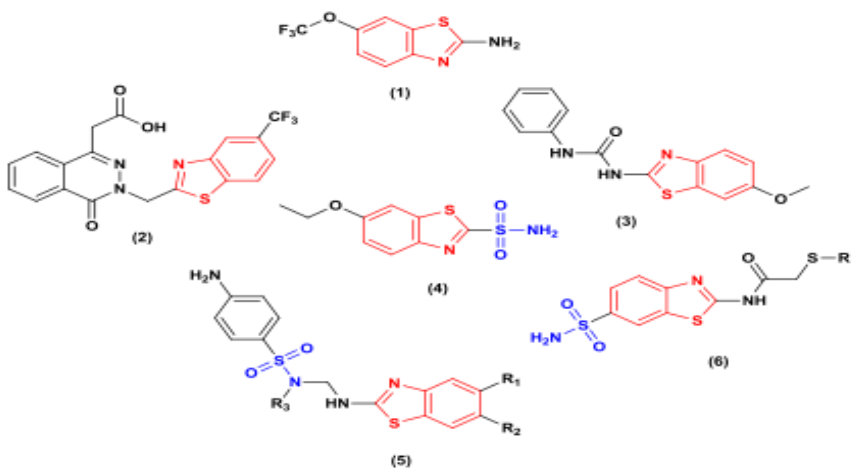


Fig.7; Some molecules with both sulfonamide and benzothiazole moieties

The appropriate synthesis of these compounds has recently drawn a lot of interest due to their diverse spectrum of biological action, which has led to the development of better methods for clean, gentler, and high-yielding techniques. The synthesis

of new benzothiazoles with sulfonamide or other heterocyclic moieties using the Cesium salt of Wells-Dawson hetero-polyacid ($Cs_5HP_2W_{18}O_{62}$) as a solid catalyst and water as the solvent under ultrasound irradiation has recently been reported as an efficient and practical protocol. The use of ultrasonic irradiation to catalyse the reaction speed was impressive. Additionally, this strategy presents several other advantages including operational simplicity, increased yields, and energy performance. [17] Thus, a cross-breed molecule containing sulfonamide and thiazolidinedione nucleus is believed to be insistent, and synthesizing such molecules under environmentally benevolent conditions is an expense to explore.

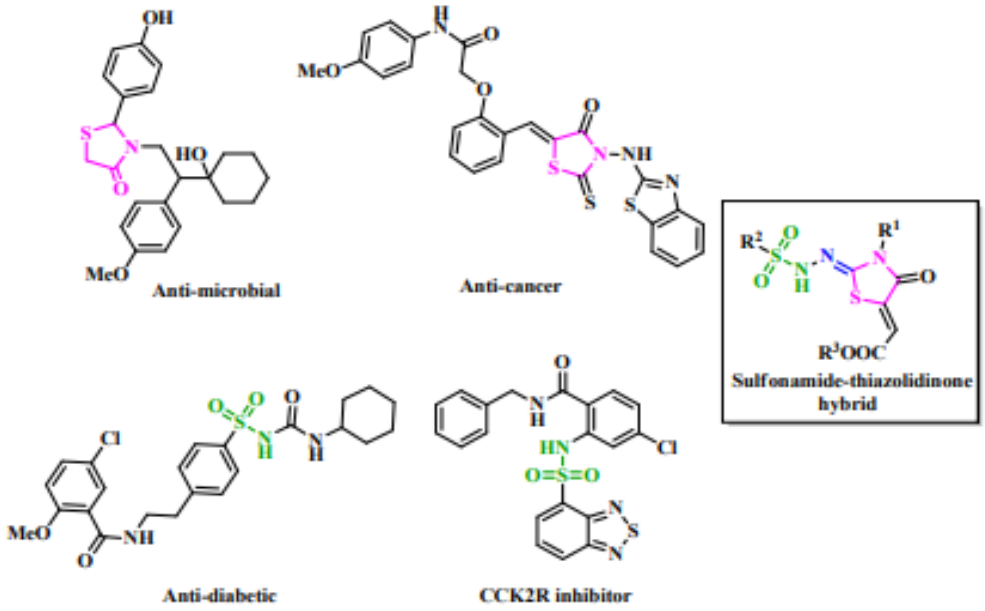


Fig.8; Sulfonamide/thiazolidine nucleus and the designed molecule

Multicomponent reactions (MCRs) are characterized as "one-pot" processes that engage at least three components at once and give priority to the end products, which should ideally contain all of the atoms of the beginning elements. As a result, MCRs have shown to be a potent tool in combinatorial chemistry due to their simplicity, effectiveness, atom-friendly design, and automation responsiveness. These outstanding benefits have made the development of new MCRs with green functionality a recurrent issue in modern chemical synthesis and drug discovery. [18] And while additional techniques have been published for making sulphonamide derivatives from various starting materials, there is still a strong need for the development of effective, straightforward, and more experimental techniques that may be used in environmentally friendly ways. The use of ultrasound as a potent tool in synthetic organic chemistry has recently proven incredibly effective and alluring. The use of ultrasonic technology accelerated the rate of organic reactions and the production of purer products in large yields and with minimal reaction conditions. In addition, compared to conventional procedures, it is regarded as a processing help in terms of energy reduction and waste minimization. In response to the aforementioned biological and medicinal properties of benzothiazole derivatives, as well as part of a larger effort to create novel heterocyclic molecules. We provide a detailed description of an effective method for producing a unique series of new benzothiazole derivatives utilizing ultrasonic irradiation and the Wells-Dawson hetero-polyacid ($Cs_5HP_2W_{18}O_{62}$) catalyst.

Recent research has described the use of the latter catalyst for the production of cyclic imides with the sulfonyl group and substituted N-acyl sulfonamides. It not only provides the goods with good to exceptional yields, but it also tackles problems related to catalysts, including pollution, safety, and simplicity of handling and recovery. We thus go over these techniques below:

Synthesis in One Pot

One-pot synthesis is a quick and easy method for creating functional nanoscale organic or inorganic crossbreed materials. The inorganic components are produced using a direct reaction in a single step, while the organic component serves as a surface-capping substance or skeleton.

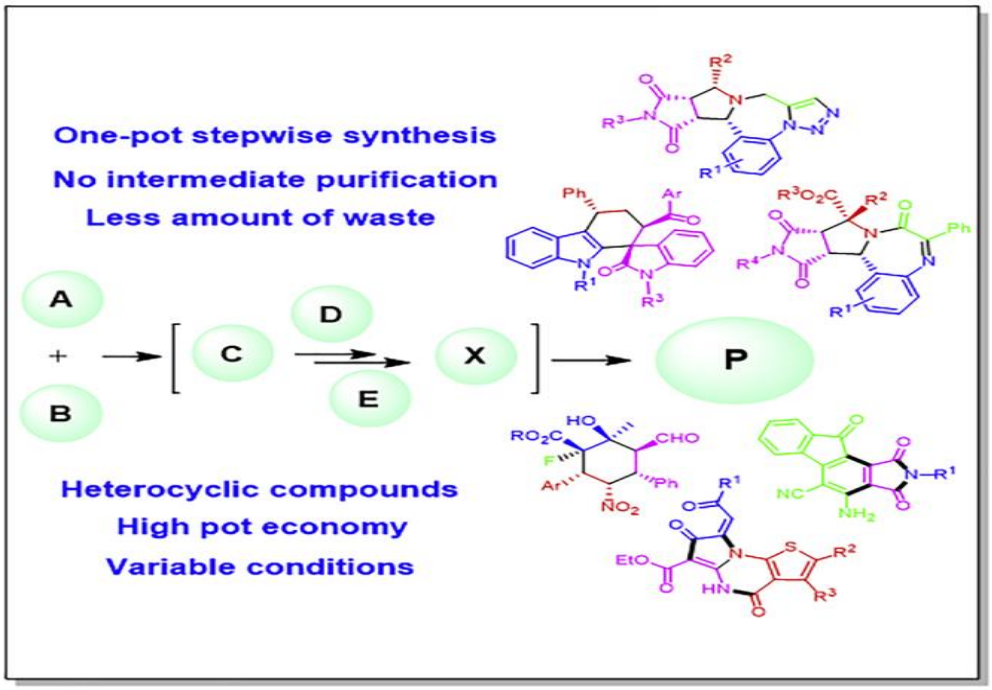


Fig.9; One Pot Synthesis

Natural scientific experts are keen on one-pot blend due to its inborn advantages of usability, high mass proficiency, modest expense, and negligible garbage removal. Among three sorts of one-pot blends,
1) overflow responses,
2) multicomponent responses (MCRs)
3) one-pot stepwise blend (OPSS)
Because of its successive interaction and changing response conditions for each stage, OPSS might be more versatile and valuable. The most recent progressions in OPSS including cyclization, cycloaddition, improvement, and reactant processes for the blend of heterocyclic platforms, deviated particles, normal items, and bioactive synthetic compounds are feature this perspective paper utilizing explicit models. [19]

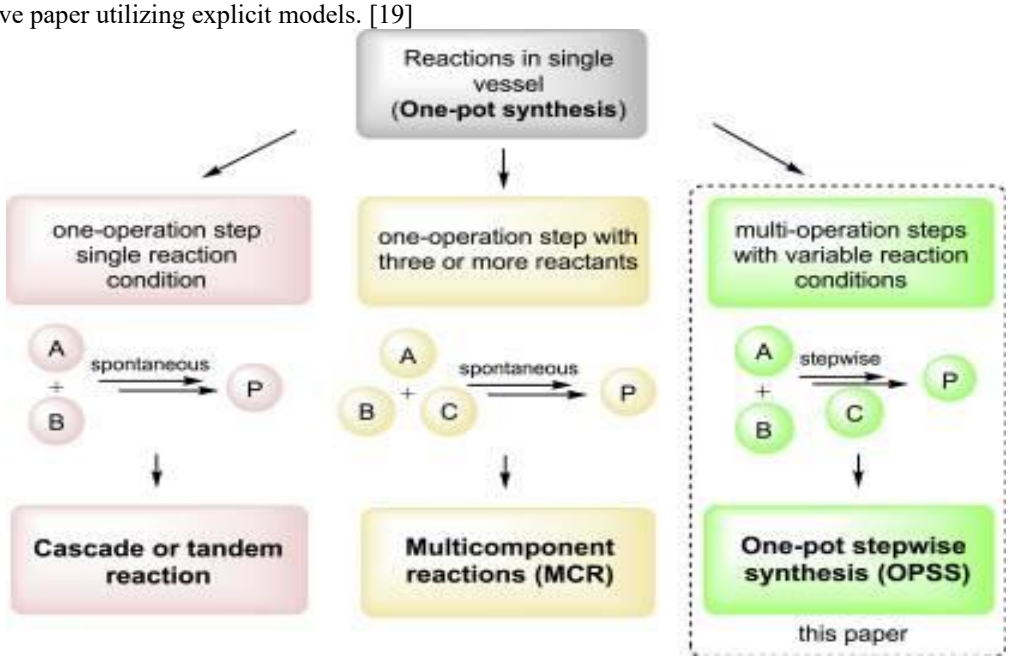


Fig.10;Types of One-Pot Synthesis

The accompanying potential misconceptions might be tried not to characterize the one-pot responses given the showed functional methodology:
1) A solitary activity response including one reactant (intramolecular) or two reactants (intermolecular) and consecutive synthetic changes ought to be alluded to as a fountain response instead of a multistep response;
2) a solitary activity response including at least three parts ought to be alluded to as an MCR as opposed to a one-pot response;

3) a one-pot response including numerous tasks steps ought to be alluded to as an OPSS as opposed to an outpouring
4) A one-pot blend with at least three parts ought to be alluded to as OPSS as opposed to MCR. [19]

Ultrasonic Irradiation Method

Organic transformations take place under ultrasonic irradiation in high yields, with swifter reaction times, or under softer conditions. Growingly, organic processes are accelerated using ultrasonic-assisted technology, which is also a green synthetic method.

Ultrasonication is the most common way of disturbing a fluid example by presenting it to ultrasonic (>20 kHz) waves. It is a notable eco-natural innovation in green science because of its benefits over the regular warm methodology, including quicker response rates.

It is widely known that ultrasonic innovation might be utilized to make green cycles, speed up synthetic responses, and other significant assignments. Further advantages are the effortlessness of the exploratory methodology, better returns and rates, more limited response times, and a clean nature. [20]

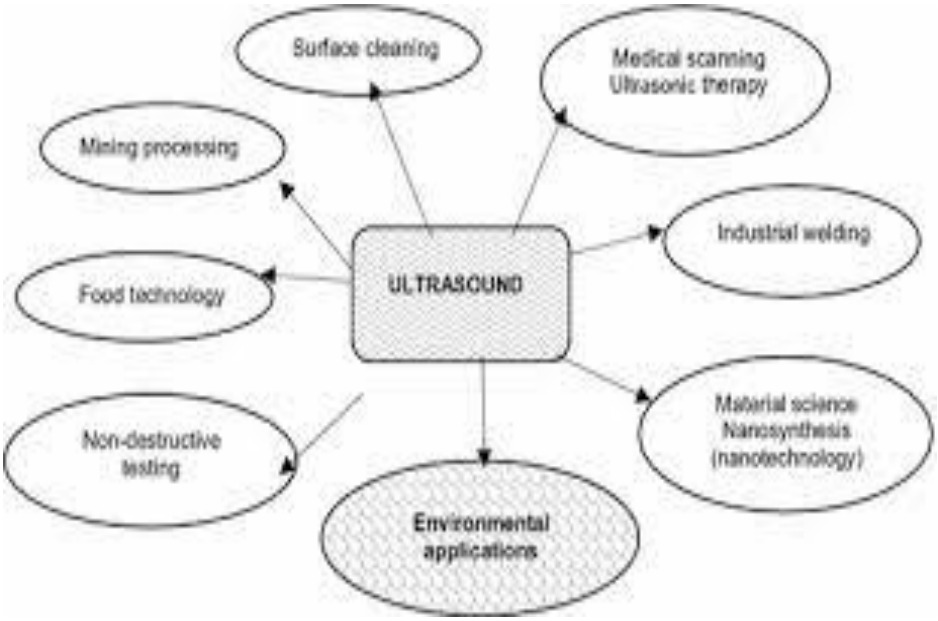


Fig.11; Applications of Ultrasound Method

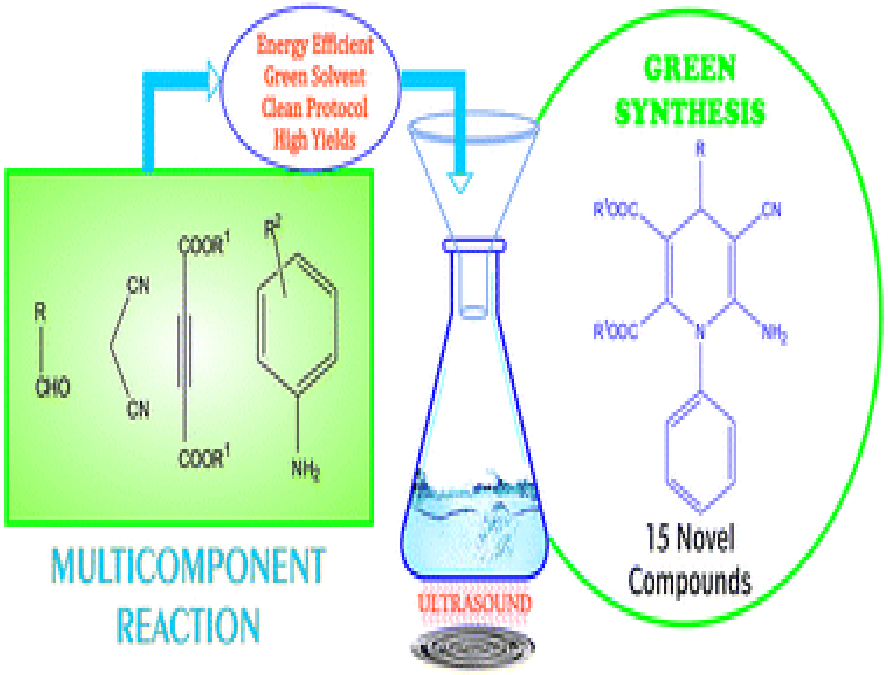


Fig.12; Synthesis of novel drugs from green synthesis

The previous literary survey particularly emphasizes the synthesis of sulfonamide moieties with heterocyclic compounds under environmentally benign conditions.[21] The use of the green medium, non-hazardous reactants, and the isolation of the products by straightforward extraction and precipitation are some of this procedure's benefits. A range of primary, secondary, and tertiary sulfonamides was produced via reactions between sulfonyl chlorides and amines in a flow meso-reactor using 'NaHCO3' as a base in a solution of 'H_2O/acetone/PEG-400'(1:2:1)[v/v/v].

Dissimilar methods are used to characterize synthesized nanosphere, such as UV-Vis spectrophotometry, which is used to validate the formation of NPs before the mixture is centrifuged and the pellet is dried in a hot air oven, to produce the crystal NPS.[22] Additional characterization techniques for synthesized compounds include the use of'X-ray diffractometer' (XRD), 'Energy Dispersion Analysis of X-ray' (EDAX), Fourier Transform Infrared Spectroscopy (FTIR), 'Scanning Electron Microscopy' (SEM), 'Transmission Electron Microscopy' (TEM), 'Field Emission Scanning Electron Microscopy' (FESEM), 'Atomic Force Microscopy' (AFM), 'Thermal-gravimetric Differential Thermal Analysis' (TG-DTA), 'Photoluminescence Analysis' (PL), 'X-ray Photoelectron Microscopy' (XPS), 'Raman Spectroscopy', 'Attenuated total reflection' (ATR), 'UV-Visible Diffuse Reflectance Spectroscopy' (UV-DRS), and 'Dynamic Light Scattering' (DLS). [23,24]

Research Problems

According to research papers, nanoparticles are having many different types of activities which are responsible for deteriorating unwanted and hazardous substances during synthesis under the condition of green chemistry. These nanoparticles are also produced using natural materials, such as plant parts like leaves, fruits, and rhizomes, as well as other biosynthesis methods, which have been referred to as "green synthesis." Because nanoparticles are produced using natural sources including plant extract, bacterial, fungal, and algal, there are certain downsides to this synthesis, including the fact that it takes longer than chemical synthesis to complete. We must provide time for the generation of culture medium, bacterial development, and the extraction of plant sources for these approaches' purposes. However, the formation of nanoparticles like Silver nanoparticles (AgNPs) mediated by *Momordica Charantia* Fruit Extract exhibits action against human lung cancer cell lines. *Momordica Charantia* FE's IC50 (half maximal inhibitory concentration) against A549 cells in the current study is 102 mg/ml, whereas AgNPs' IC50 is 51.93 mg/ml. The found IC50 value was 76.92 mg/ml, indicating that as-synthesized AgNPs display high anticancer activity against lung cancer cells, contrary to beforehand publications' findings that the IC50 value of 51.93 mg/ml against the A549 cell line revealed improved biocompatibility. AgNPs' anti-cancer effectiveness can be sorted as follows: A549 > HOP-62 > *Momordica Charantia* FE **[10]**(shown in fig13,14)

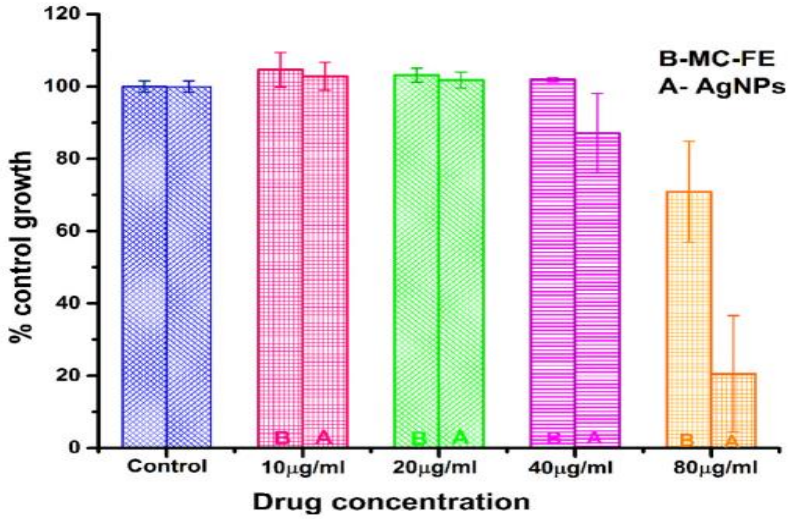


Fig.13; *In-vitro* cytotoxicity studies for *M. charantia*fruit extract (MC-FE), which is represented by **B** and *M.charantina* established silver nanoparticles (AgNPs), which is shown by **A.**

In the plot increasing the concentration of AgNPs (10-80 µg/ml) on the X-axis inhibits the viability of cells on the Y-axis.

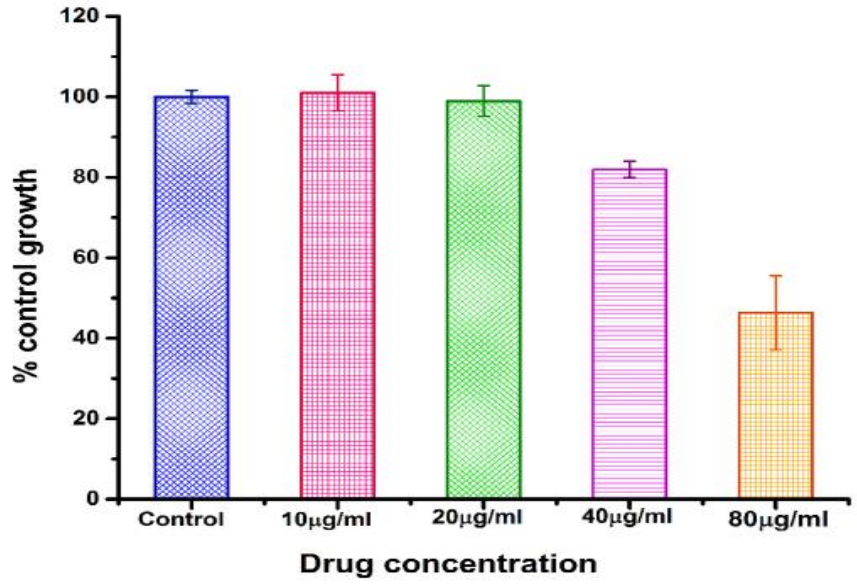


Fig.14; *In-vitro* cytotoxicity studies for *M. charantia-derived* AgNPs against HOP-62 lung cancer cell line [11]

In other investigations, it was found that the cytotoxicity of greenly incorporated AgNPs was surveyed utilizing the MTT test and that, at centralizations of 25-500 µg/mL, it displayed an enemy of malignant growth activity against colon disease (HT29) cells. (Fig15). Since AgNPs were assessed at a few focuses including 25, 50, 100, 250, and 500 µg/mL, the required fixation to decrease the suitability of HT29 cells to half (IC50) of the underlying populace was 150.8 mg/mL. (Fig 14) The ongoing examination for the counter colon malignant growth activity of AgNPs blended using rhizome concentrates of *Curcuma longa* and *Zingiber officinale* was distributed in 2013 and reports that a characteristic polyphenol particle viewed as in C. longa hinders the augmentation of a few growth cells, including bosom disease. In this manner, an expanded portion of subordinate human cytotoxicity is the forthcoming issue. So as per this approaching issue higher portion subordinate cytotoxicity of human colon carcinoma cells after 24 hr of AgNPs treatment.**[12]**

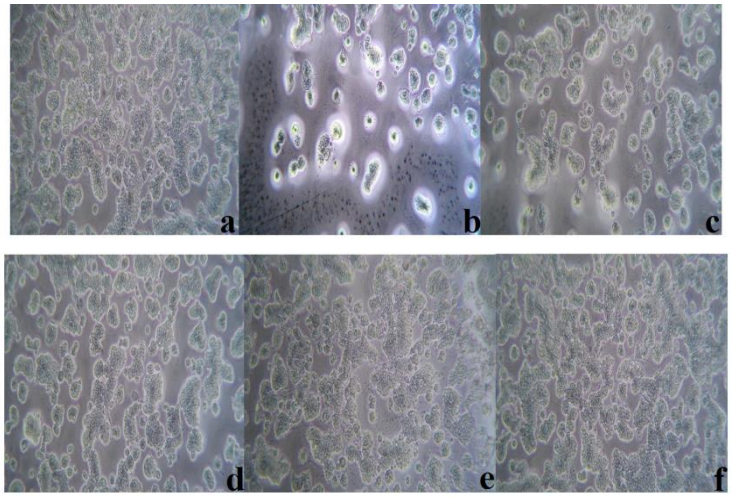


Fig.15; Anticancer activity of Zingiber officinale and Curcuma longa silver nanoparticles
a) control, b) 500µg/ml, c) 250µg/ml, d) 100µg/ml, e) 50µg/ml and f) 25µg/ml

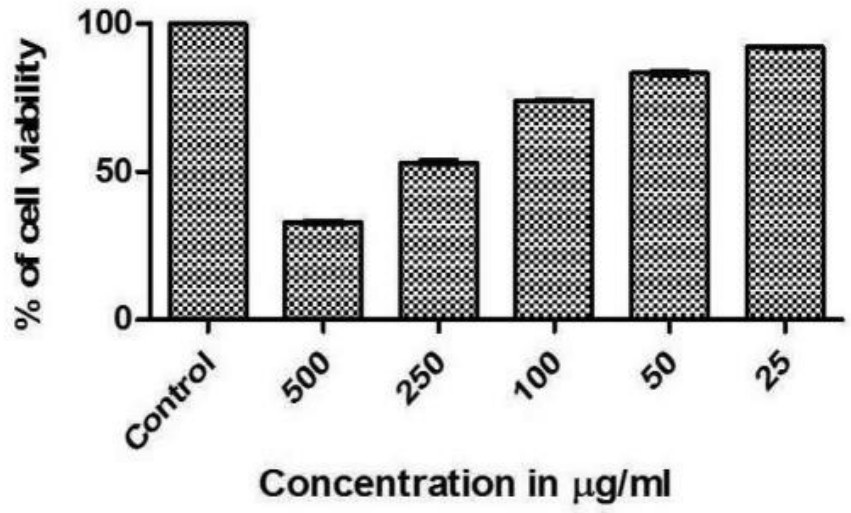


Fig.16; *in-vitro* cytotoxicity effects of green synthesized AgNPs

And further studies I got a problem again dose-dependent. 'MCF-7' cells were given different dosages (0, 12.5, 25, 50, and 100 g/mL) of Ag-NPs created using "S. Alexandrina" leaves extract to test their cytotoxic potential. The results showed that 'MCF-7' was not significantly cytotoxic to lower dosages of Ag-NPs (12.5 and 25 g/mL). Ag-NPs did, however, exhibit significant cytotoxicity at the greatest concentration of 100 g/mL (Fig. 17). When evaluated against MCF-7, Ag-NPs' IC50 value was shown to be 61.93.8 g/mL. [7]

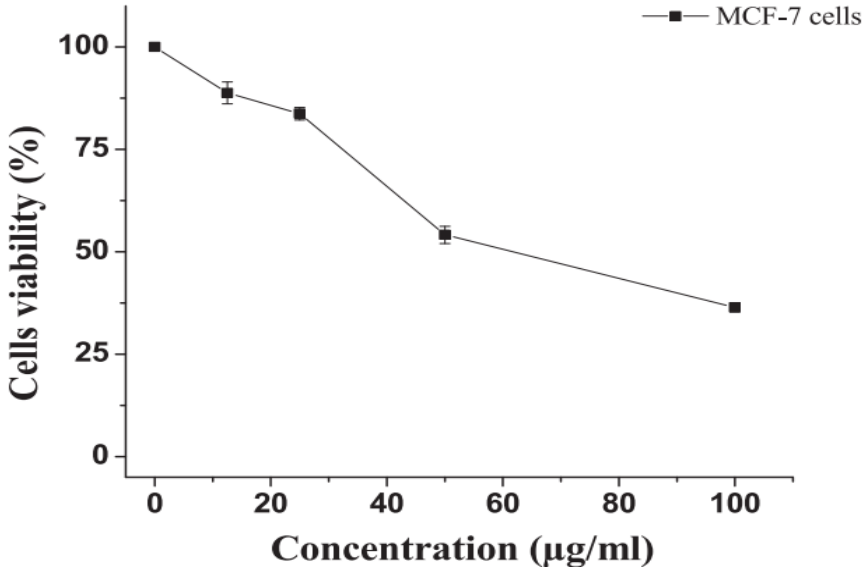


Fig.17;*S. Alexandrina* leaves extractcytotoxicity potential

And again, got the same problem that is dose-dependent. 'Lung carcinoma cells' (A-549) and 'ordinary lung cells' (WI 38) were surveyed for the cytotoxicity of 'TMC/Ag' nanocomposite. The nanocomposite showed portion subordinate cytotoxicity against 'A549 cells' with 'IC50' of 12.3 µg/mL, though the 'IC50' esteem against typical WI 38 cells was 357.2 µg/mL [8]

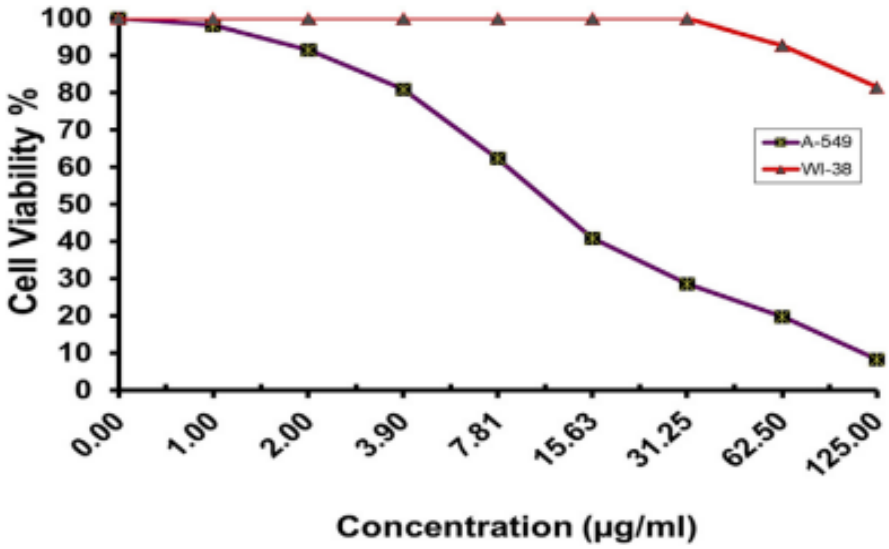
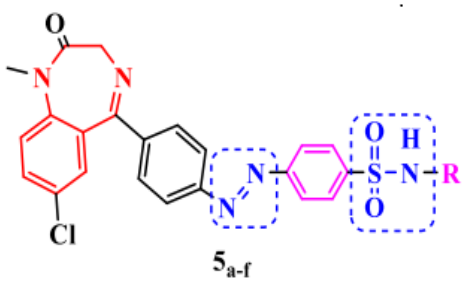


Fig.18; Cytotoxicity effects of TMC/Ag nanocomposite on A-549 and WI-38 cells

Additionally, the study issue was approached from two separate perspectives—"bottom-up" and "top-down"—using several procedures, including traditional and innovative ones. Even though there are many conventional ways to make AgNPs (like arrangements, substance and photochemical responses in turn around micelles, warm decay of different silver mixtures, electrochemical, sonochemical, radiation, and microwave-helped strategies),they typically involve dangerous chemicals, high energy demands, and inefficient purification processes. AgNPs may now be produced using green chemistry and biosynthetic techniques, which have grown in popularity recently. These unorthodox techniques either employ various alcoholic or aqueous plant extracts or biological microorganisms (such as bacteria, fungus, sea algae, and yeasts). Most of those methods have certain drawbacks, such as difficult setup procedures, low product yields, costly and unfavourable catalytic reagents, and in some cases, catalysts that are bad for the environment and cannot be recycled. Consequently, moderate reaction conditions in a non-catalyst process are still preferred. In chemical synthesis, environmental conditions for reaction, extraction, and purification are perpetually sought to minimize the impact of dangerous solvents and chemicals on nearby plants and animals. Additionally, future issues with nanoparticle size, shape, and structure cannot be prepared in the same way. Depending on the procedures utilized, the sources used the environment, temperature, solvent, etc., different forms and sizes are discovered. Because green synthesis produced a large number of nanoparticles through green synthesis have the same shape but size & sources different. So as per this, we cannot easily identify which nanoparticles are synthesized by which sources. We have demonstrated that different sources may produce metal nanoparticles with different dimensions, shapes of nanoparticles like spherical, spike, needle, colloidal, etc., and dosages form of nanoformulations. Another part of this study which is included the synthesis of sulphonamide derivatives with heterocycle under green chemistry. I saw a few drawbacks to using sulphonamide that can cause toxic effects and harmful effects on the environment induced during drug formulation.

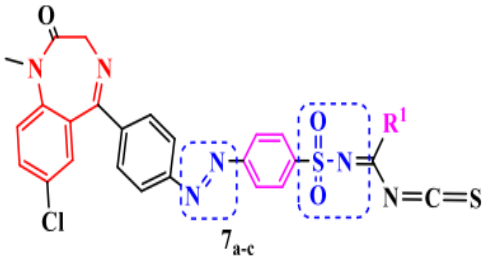
Instantly, it is removed bilirubin from transported protein albumin in human beings, and then induced to the level of bilirubin in the body, which causes toxicity in the CNS, liver & kidneys. [25] The expulsion of squanders from their amalgamation can likewise be unsafe to the climate because of the broad utilization of natural solvents (for example dimethyl formamide) or profoundly receptive harmful beginning materials (for example thionyl chloride). As referenced over all organic activities of sulfonamide subordinates depended on a solitary objective technique. The generally single-target drugs with high unambiguous movement have been created when tried in-vivo, furthermost will more often than not have a high pace of disappointment. This prompts diminished drug action and a higher opportunity of poisonousness since higher portions or treatment with different medications may be required while utilizing single-target drugs. [25]

It recently revealed that "Sorafenib"& "Doxorubicin" utilized as reference cytotoxic medications against the blended mixtures showed higher affinities towards 'VEGFR-2'. It uncovered that compound '5a' showed lower fondness and compound '7(a-c)' shows almost equipotent affinities in contrast with "Sorafenib". The distal moieties shaped Hydrogen and lipophilic holding communications and subsequently affinities towards the 'VEGFR-2' chemical. Extension of the design assumed a significant part in their 'VEGFR-2' inhibitory exercises. The diazene and sulfonamide linkers framed hydrogen holding communications which expanded proclivity towards the VEGFR-2 catalyst. [15]



5_{a-f}

a. R=H
b. R= pyrimidin-2-yl
c. R= 4- methylpyrimidin-2-yl
d. R= 4,6-dimethylpyrimidine-2-yl
e. R= 5-methylisoxazol-3-yl
f. R= quinoxaline-2-yl



7_{a-c}

a. $R^1 = CH_3$
b. $R^1 = C_6H_5$
c. $R^1 = C_6H_4(2\text{-}Cl)$

7a-7c

It revealed also that distal & heteroaromatic motifs when acquainted with other phenyl tails like sulphonamide of the reference covalent holding with various lipophilicity then, at that point, shows their impacts on anticancer action. Sulfonamide goes about as a linker to upgrade the length of the design to distal themes to frame new lipophilic and H-holding communications with the separate receptor. This point makes sense of the recently integrated compounds showed various impacts of anticancer movement specifically against the 'MCF-7 cell' lines. Since linkers like hydrogen-restricting acceptor and hydrogen-restricting benefactor (HBA-HBD) are generally lipophilic they assume a part in anticancer action. So as per this idea, the supplanted sulfonamide linker as in intensifies 5(b-f) showed higher exercises than the unsubstituted one as in compound 5a against the three 'Hep-G2', 'HCT-116', and 'MCF-7 cell' lines. This implies the impending issue that main subbed sulfonamide linkers show more strength against destructive cells because of their stretching design of subordinates. [15]

In the second gathering '7(a-c)' the distal electron lacking phenyl ring subbed with lipophilic electron pulling out chloro bunch as in compound '7c' displayed higher exercises than that unsubstituted phenyl one '7b' and the aliphatic electron-giving methyl one '7a' against the three 'Hep-G2', 'HCT-116', and 'MCF-7 cell' lines.

Thus, after completely referencingthe above examinations I found a forthcoming issue that significant point is the dose detailing of nanoparticles, single designated drug conveyance is harmful, and unsubstituted sulphonamide subordinates have low viability against anticancer movement. Also, different focuses connected with the biocompatibility and well-being profiles of silver nanoparticles and sulphonamide subordinate drugs are basic for their expected clinical application. Broad exploration has shown that appropriately designed 'AgNPs' can display biocompatibility while keeping up with their anticancer properties. Be that as it may, exhaustive poisonousness assessment and dose advancement are fundamental to moderate expected unfriendly impacts.

Solution Found

The synergy between silver nanoparticles and sulphonamide derivatives in anticancer activity can be attributed to multiple factors. 'AgNPs' can enable the uptake of sulfa drugs into cancer cells, enhancing their intracellular accumulation and promoting localized drug release. Also,' AgNPs' can extend the apoptotic effects of sulphonamide agent through modulation of cellular redox balance and dislocation of tumor cell membrane integrity. The combined action of 'AgNPs' and sulfa drugs results in greater anti-proliferative effects, increased cancer cell apoptosis, and reduced drug resistance.
Recently the study mentioned over is although revealed by choosing environmentally friendly settings, such as greener methodology that uses rarer chemicals, low cost, favorable conditions, harmfulness of ecologically gentle solvents, usage of catalytic agent, etc.

So, the synthesized greener Silver nanoparticles are derived from natural sources using various parts and revealed different pharmacologic activities like anticancer with good productivity, good profit, and better potency of activity. It is inexpensive and needs little upkeep, plants are known as the chemical factories of nature.

They have advantages such as a quick generation time, simplicity in culture, amiable experimental settings, exceptional stability, creation of extracellular nanoparticles, and simplicity in genetic modification. It is a type of unconventional method or synthesis. The conventional synthesis used for the treatment of cancer cells like chemotherapy, irradiation, or surgical procedure will induce damage to malignant cells as well as strong cell also. So using unconventional methods like

green chemistry is helpful for this problem and is treated with low toxicity, less hazardous chemical use, eco-friendly, and low cost.

That's why we used greener nanotechnology for cancer treatment which is more potent and effective with fewer adverse effects than traditional treatment as the conventional system. [2]

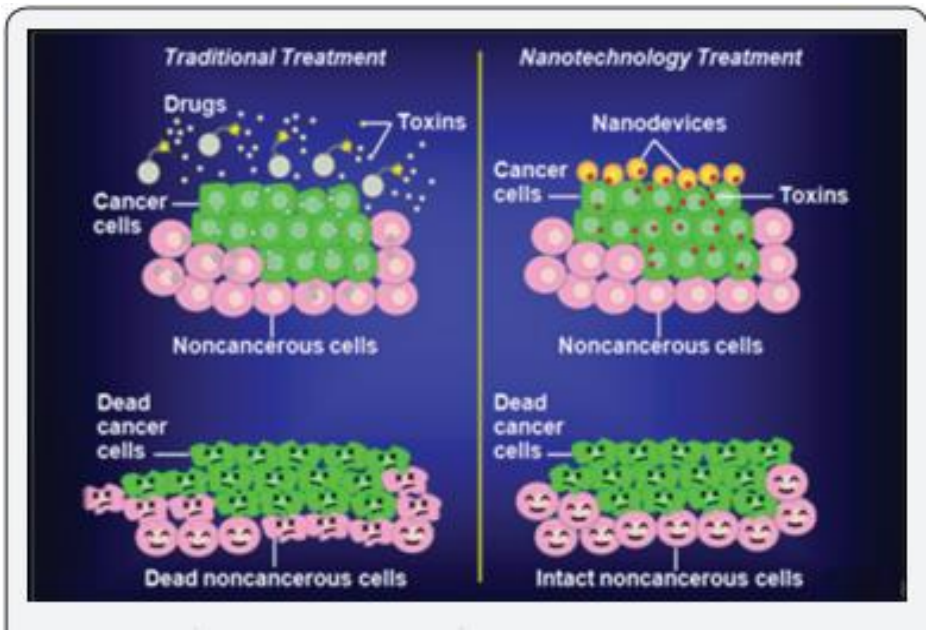
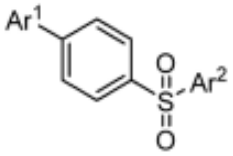


Fig.19; Comparative study of Traditional and Nanotechnology Cancer Treatment

Drugs may be easily synthesized with the use of nanoparticles and have high purity and effectiveness. As of late, encouraging procedures for making sulfonamide compounds in "green condition" or non-harmful way without the utilization of natural solvents. As indicated by momentum research, multi-target compounds seem to have more noteworthy revealed movement than single-target drugs. The 'sulfonamide' subsidiaries that are expected to work on a few targets associated with a specific disease are commonly found to have diminished poison levels alongside lower 'IC50' or 'EC50' values, which is an enormous assistance in delivering medicines that would require negligible dosages and have the least secondary effects conceivable. Other muddled messes, like malignancies and growths, have additionally been dealt with utilizing sulfonamide subsidiaries with multi-focusing on capacities (Fig. 18). As a matter of fact, their utilization in growth and disease medicines goes as far back as (2010) Marques et al. detailed the utilization of 'pteridine-sulfonamide' forms for their true capacity as antitumor specialists with the capacity to forestall both carbonic anhydrases and dihydrofolate reductase. They tried the diamino pteridine-benzenesulfonamide subordinates against the slight cell lung carcinoma, 'A549', and prostate carcinoma, PC-3, and got millimolar range exercises, showing the requirement for development.



Ar^1	Ar^2
NHCS-linked phenyl derivatives	chromen-2-one derivatives
ketone or aldehyde long chains	phenyl derivatives
H	methylthiazoloisoxazole derivatives
p- or *m*-Cl and F	nipecotic acid or β-alanine derivatives
m- or *p*- $NHSO_2NH_2$	
amino acids	

Fig.20; General structure of sulfonamide compounds with potential anticancer activities

In above studies reported that the sulphonamide acts as a linker that initiates the structure elongation through ring expansion & bioisosteric modification process. It promotes the lipophilic nature of the drugs, due to this the anticancer activity of drugs becomes more potent and more effective as well as less toxic. According to the above studies all synthesized drugs showed variable activity against different cancerous cell lines.

However, the information from the docking experiments and the results of the biological screening were strongly linked. The 'MCF-7' cell line was the one that responded to the novel compounds' effects the greatest. With 'IC-50' values of 8.98 ±0.1µM, 7.77 ±0.1µM, and 6.99 ±0.1 µM against the three 'Hep-G2', 'HCT-116', and 'MCF-7'tumourcell lines, correspondingly, complex '5d' was discovered to be the most potent derivative overall of the examined complexes. Complex'5d 'was more active than "Sorafenib" against 'HepG2 and MCF-7' cancer cell lines, but less active against 'HCT-116'tumour cell lines (IC50 = 9.18 ±0.6µM, 5.47 ±0.3µM, and 7.26± 0.3 µM, respectively). Additionally, this drug was less active than "Doxorubicin" against 'Hep-G2' and 'MCF-7' (IC50 = 7.94± 0.6µM, 8.07 ±0.8µM, and 6.75 ±0.4 µM, respectively), although higher activity against 'HCT-116 cell' lines correspondingly.

Additionally, complexes'7c and 7b'substantiated potent 'VEGFR-2' inhibitory action with 'IC50 values' of 0.16 ±0.06µM and 0.17± 0.06 µM, one-to-one. These values are greater than half of "Sorafenib's biological activity. With 'IC50' values of '0.29± 0.06µM and 0.32 ±0.06 µM', respectively, compounds '7a and 5a' showed moderate 'VEGFR-2' inhibition.

Conclusion

The importance of developing stable, economically viable, environmentally benign silver nanoparticles has increased as a result of biological synthesis in the field of nanobiotechnology. In electronics, agriculture, and medicinal chemistry, these particles are used in a variety of applications. Numerous studies on the creation of nanoparticles using nanotechnology have demonstrated that utilizing natural plants is safer and more effective. Despite an enormous variety of plants, many more have not yet been looked into for their potential for generating nanoparticles and be used in industries such as food and medicine.

The synergistic effects of silver nanoparticles and sulphonamide derivatives in anti-cancer activity present a promising approach for improving cancer treatment outcomes. Their combined action offers advantages such as enhanced anticancer efficacy, reduced drug resistance, and minimized side effects. However, further research is necessary to fully elucidate their optimal usage, evaluate their safety profiles, and translate these findings into effective clinical applications.

Rapid advancements in microengineering have led to the constant development of new ways to obtain tiny particles. Environmentally sustainable approaches for the production of nanospheres have drawn a lot of interest in the last 10 years, particularly because traditional chemical procedures result in dangerous byproducts. The production of nanoparticles with various sizes and morphologies involves organisms ranging from straightforward bacteria to more complicated eukaryotes, as well as several plant extracts. In comparison to other biological entities, the production of nanoparticles using aqueous or alcoholic plant extracts offers several benefits, especially since cell cultures are not required. Evenly occur many literature publications on the green synthesis of nanoparticles; there is still a great deal of study being done on plant extracts as prospective scholars for the anabolism of nanoparticles. Various types of physicochemical methods were used to analyze every nanoparticles, and different physicochemical methods and all of the findings demonstrated that synthesis occurs with predictable results. Antimicrobial efficacy and antioxidant capabilities were also examined. An efficient and feasible alternative is produced by the presented method for the synthesis of sulphonamide with a heterocycle, which proceeds under ultrasonic wave irradiation. The findings demonstrate that the one-pot reaction, which used water as the green solvent and the cesium salt of the Wells-Dawson hetero-polyacid (Cs5HP2W18O62) as the catalyst, was efficient and yielded the intended Benzothiazole with good to exceptional yields that included sulfonamide or cyclicimide moieties. The suggested strategy was straightforward and ecologically responsible.

In this review, we specifically addressed the ecologically safe production of sulfonamide moieties. Researchers in this discipline are putting considerably more effort into screening the use of ecologically friendly solvents to boost the greenness of sulfonamide manufacture. The main thrust of research in this area of green approach is on conducting reactions either in an aqueous media or under neat reaction circumstances. Froman environmental perspective, pharmacists are also extremely cautious about refusing to utilize metal for the production of sulfonamide. A thoughtful evaluation of the mechanistic elements also adds flavor for the readers and enhances the green chemistry-based process for synthesizing pharmaceuticals employing nanoparticles as catalysts. We anticipate that this review will be quite fascinating for active researchers. This methodology has a higher yield, shorter reaction time, green conditions, and optimization of the motif of the synthesized compounds are the major advantages of the method. The structures of the synthesized derivatives were carefully characterized by X-ray determination, ^{1}H, ^{13}C NMR as well as IR. Swiftly and autonomously. It is commonly acknowledged that nanotechnology may one day be used to treat illnesses. Due to the huge variety of biodegradable organically dynamic metabolites that are present in significant amounts in plant removals, the biogenesis of nanosphere from herbal extracts is gaining a great deal of attention.

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