Abstract: Recently, researchers succeeded in designing and manufacturing a new class of nanoparticles (NPs) called hybrid NPs. Among hybrid NPs, bimetallic and core–shell NPs were a revolutionary step in NPs science. A large number of green physiochemical and methods for nanostructures synthesis have been published. Eventually, physiochemical methods are either expensive or require the use of chemical compounds for the synthesis of bimetallic and core–shell nanostructures. The main challenges that scientists are facing are making the process cheaper, facile and eco-friendly efficient synthesis process. Green synthesis (biosynthesis) refers to the use of bio-resources (such as bacteria, fungi, plants or their derivatives) for the synthesis of nanostructures. The popularity of the green synthesis of nanostructures is due to their environmental friendliness and no usage of toxic materials, environmental friendliness for the synthesis or stability of nanostructure. Bimetallic and core–shell NPs have many biomedical applications such as removing heavy metals, parasitology, molecular and microbial sensor, gene carrier, single bacterial detection, oligonucleotide detection and so on. The purpose of this study is to discuss briefly the biosynthesised bimetallic and core–shell NPs, their biomedical applications.

1 Introduction

Nanoparticles (NPs) are defined as a particle with size range in 1–100 nm, at least for one dimension [1]. Materials that are sized at NPs are about 1000 times smaller than microsized (micronsized) particles (Fig. 1). NPs have shown novel biological and physicochemical properties [2–8].

At first, the main focus of scientists was the synthesis and application of NPs that contained single structures, called simple NPs such as silver, gold and selenium, due to their unique features and utilisation [9–17].

The improvement of knowledge has helped scientists to design a new class of NPs known as hybrid NPs, which can be defined as well-organised nanomaterials consisting of two, three, or more types of single nanocomponents [18]. Core–shell NPs are a kind of hybrid NPs that are also written as core/shell, core–shell, and core@shell NPs. Core–shell NPs are composed of two or more nanomaterials, which includes a wide range of organic and inorganic nanomaterials (metals or polymers), while one of them acts as a core and the other nanomaterial is located around the central core called shell (Fig. 2). Bimetallic NPs composed of two different metal elements [19].

The knowledge of hybrid NPs synthesis stands as a revolutionary step in the nanoscience. The ability to manipulate NP's structure has helped us in producing a large number of hybrid NPs [20–25]. The core–shell NPs with the ability to be utilised in a wide range of materials as core or shell can represent its satisfying unique features and custom functions. Depending on the purpose of the study, core or shell materials can be selected [26]. The properties of core–shell NPs can be altered by inducing changes in the ingredients that constitute the core or shell layer. Features and distinctive properties including physicochemical, biological, optical, etc. can be observed when different nanomaterials are combined such as core shell NPs. These hybrid NPs are employed in designing applicable programs in different fields such as medicine, engineering and so on [27–31].
Synthesising NPs, yet researchers are not interested due to its disadvantages, yet the green synthesis methods have proven to be cost-effective, environmentally benign and easier than physiochemical methods. Nature has provided millions of bio-resources that these particular bio-resources contain a large variety of biomacromolecules in their extract which participate in their own physicochemical characteristics of NPs helps to effectively understand the relationship between these characteristics and their performance. From previous studies, the antimicrobial efficiency of silver NPs with smaller sizes seem to be more than that of the larger sizes. Describing the behaviour and structure of green synthesised NPs is quite difficult due to the existence of various macromolecules in their extract which participate in their own structure.

### 2 Different synthesis methods of hybrid (core–shell) NPs

A large number of bottom-up and top-bottom approaches have been reported for the synthesis of various nanomaterials. In the bottom-up approach, self-assemble type of atoms led to the formations of nanosized particles; but in top-bottom approach, bulk materials are broken down to nanosized particles (has not been yet put under investigation for core–shell NPs). Although the top-bottom approach is an applicable technique, yet the bottom-up methods are preferred.

Regarding the synthesis of core–shell NPs, three step approaches have been reported:

i. **One-step**: The core and shell are formed together.

ii. **Two-step**: The core is synthesised first, then the shell layer is formed around the synthesised core surface.

iii. **Multiple-step**: The core is synthesised first, then the first shell layer is formed around the synthesised core surface and finally a second shell layer is set up on the first shell surface or have the core removed, in which hollow-core–shell NPs can stand (Fig. 4).

![Core–shell NPs](image)

**Fig. 2** Structure of core–shell NPs

Core–shell NPs are classified into the following types (Fig. 3, [32–38]) based on the structure [26].

Each structure contains its own unique and specific properties.

### 3 Characterisation of bimetallic and core–shell NPs

Identifying and studying the physicochemical properties, structure details, purities, and dopants of biosynthesised NPs is very important as the structure, size, shape of NPs can significantly affect their performance and properties. In fact, determining the physicochemical characteristics of NPs helps to effectively understand the relationship between these characteristics and their performance. From previous studies, the antimicrobial efficiency of silver NPs with smaller sizes seem to be more than that of the larger sizes. Describing the behaviour and structure of green synthesised NPs is quite difficult due to the existence of various macromolecules in their extract which participate in their own structure.

In the following sections, common physicochemical characterisation techniques of NPs are described briefly.

#### 3.1 Spectroscopic analysis

UV–vis spectroscopy analysis is very common for primary detection of different kinds of NPs with the ability to absorb electromagnetic radiation in the UV–vis spectral region; e.g. the UV–vis absorbance of gold NPs is around 490–600 nm range.

#### 3.2 Microscopic analysis

Microscopic analyses, such as transmission electron microscopy (TEM) and high-resolution TEM (HRTEM), atomic-force microscopy (AFM), scanning electron microscopy (SEM), field emission SEM (FESEM) and analysis have been used to examine the size, morphology, and distribution of nanomaterials. AFM and SEM images are not applicable for studying the structure of core–shell NPs since they characterise the surfaces. Recognising the core in SEM images is too difficult while TEM images are very convenient for studying the structure of core–shell NPs considering its ability in measuring the thickness and spacing between core and shell/shells. Energy dispersive spectrometry (EDS) is an accessory of electron microscopy instruments (TEM and SEM). EDS is a powerful method for determining the chemical nature of the core and shell, which has displayed the distribution of elements in the studied samples.

#### 3.3 X-ray diffraction (XRD)

Scattering analysis and XRD analysis have been utilised to examine the crystal structure and phase purity of the synthesised NPs...
3.4 Fourier transform infrared (FTIR) spectroscopy

FTIR can be used to identify the surface modification of NPs, confirm the load-drug and overlay functional, identify the type of functional groups and biomolecules that are responsible for capping and efficient stabilisation of NPs, ensure the existence of shells in core–shell NPs, verify the band between the two layers of the shell in core double shell NPs, and qualitative and quantitative identification of the molecular structure of organic compounds in the NPs structure and especially in structure of core–shell NPs or hollow-core/porous-shell materials.

3.5 Thermal gravimetric analysis (TGA)

TGA is a thermal analysis by which the mass of an NPs is measured over time as the temperature changes (usually between 25 and 800°C). Also, the properties of the oxidation resistance of...
the core–shell NPs can be tested by the TGA. For example, Ammar et al. illustrated that the weight increment of the coated particles caused by FeNi oxidation decreased from 20 to 4%, which is relative to that of the uncoated FeNi particles using TGA. This analysis can be utilised to determine the structure of core–shell NPs, hydration, effective absorption of drugs in mesopore NPs, and measuring the magnetic performance of hybrid NPs. TGA measurements can be performed under different atmospheres such as air, hydrogen, ozone, and argon. We can ascertain the amount of organic molecule residues in the structure of NPs through the TGA analysis in ozone. Significant weight loss in the mass of green synthesised NPs at high temperatures is due to the degradation of biomolecules in the structure of NPs, considering how the biomolecules in the extract play the roles of both capping and reducing agents.

### 3.6 Vibrating sample magnetometer (VSM)

VSM can be used to study the magnetic properties of NPs. Maintaining magnetic properties, achieving higher magnetic properties, determination of the magnetic performance regarding the core–shell NPs when compared to the single structured NPs, have made it important and practicable in biology, medicine and industry applications. The magnetic Fe₃O₄: TiO₂ core–shell NPs can be applied to tumour therapy. VSM has shown the magnetic properties of iron–iron derivatives NPs with higher magnetism than iron NPs (single structure).

### 3.7 X-ray photoelectron spectroscopy (XPS)

It is very vital to identify the core–shell NPs oxidation status in catalytic systems and gas detection sensors in order to understand their chemical and physical behaviours. The surface oxidation of these NPs has been investigated via XPS analysis, which is a
technique for analysing the surface elements with a nanometre sampling depth. It can also determine the atomic ratio in NPs with heterogeneous structure and provide the chemical information of specified elements such as distinguishing between sulphate and sulphide forms of sulphur that necessary for comprehending the morphology of NPs core–shell.

3.8 Brunauer–Emmett–Teller (BET)

Precise measurement of surface area, volume, and pore distribution is important in characterising the polymers pharmaceutical materials and the coating of NPs. BET analysis was used to determine the structure of porous, as well as the shape and position of the cavities that are relative to each other within the NPs texture. The surface specific area, peculiarities of the surface, and volume of the pores of the hybrid NPs play a vital role in determining their functional activities such as the amount of drug loaded in NPs-based targeted drug delivery systems, and controlling the release of the loaded drug, absorption, storage, catalytic and so on.

4 Biomedical applications of core–shell NPs

Nowadays, nanoscience stands as one of the most attractive sciences in the world (Fig. 7). Nanoscience cannot be limited to a specific category. This particular area is an interdisciplinary field of science that can be employed for many applications [43–50]. Compared to single NPs, bimetallic and core–shell NPs with improved properties have a special economic value due to the
existing increase in their durability, performance, and breadth of applications in medicine, engineering and other industrial fields. In recent years, core–shell NPs have caught the attention of scientists due to the diversity of their structures, potential and multipurpose applications, unique structural features, simple production methods and easy control. These NPs contain several beneficial features such as the ability to function in a wide range of pH, temperatures, magnetic properties and so on [51–55].

Design and synthesis of hybrid NPs with desired structures can attract the attention of scientists toward biosynthesis hybrid NPs. The designs of suitable custom hybrid NPs and their utilisations are truly endless. Some products will be offered every day in this area while containing a very strong economic ripe. A hybrid has been known to be selective and sensitive when used as DNA, protein, secondary metabolic or enzyme markers for diagnosing pathogens cells or diseases. Medical applications of hybrid NPs help in the early diagnosis of pathogens or diseases (Fig. 8). Table 1 summarises the biomedical applications of different hybrid NPs (Table 1).

5 Conclusion

This review suggests the sustainable development in the green synthesis of all kinds of hybrids, especially core–shell NPs, which can lead to the expansion of green chemistry in near future.

The strong belief in the usage of biological resources (green synthesis) is caused by observing, chemical stability, solubility and biocompatibility of the synthesised NPs in water when compared to the conventional physicochemical methods. Green synthesis
Table 1: Some biomedical applications of different hybrid NPs

| No. | Hybrid nanostructure         | Synthesis method | Application                       | Ref.       |
|-----|------------------------------|------------------|-----------------------------------|------------|
| 1   | iron–copper bimetallic       | chemical         | degradation contaminants          | [56]       |
| 2   | Ag–Cu bimetallic            | biosynthesis     | cellular imaging                  | [57]       |
| 3   | Au–Ag bimetallic            | biosynthesis     | degradation of harmful dye        | [58]       |
| 4   | NiZnO nanocomposite         | chemical         | removal of toxic textile dyes from wastewater | [59]       |
| 5   | ZnO@polymer core–shell      | biosynthesis     | cell imaging                      | [60]       |
| 6   | Ni/ NiO core Shell          | chemical         | protein separation                | [61]       |
| 7   | Co@Au yolk/shell nanospheres| —                | gene transport vehicles, cellular optical imaging | [62]       |
| 8   | magnetic luminescent core shell | chemical   | peptide nucleic acid and DNA biosensor | [64]       |
| 9   | cobalt ferrite core–shell   | chemical         | drug carrier and cancer treatment | [65]       |
| 10  | palladium/platinum          | biosynthesis     | antibiofilm and anti-asthmatic activity | [66]       |
| 11  | Au–Ag core–shell            | biosynthesis     | drug detection                     | [67]       |
| 12  | Au–Ag bimetallic            | biosynthesis     | biosensing, bioimaging and biomedicine | [71]       |
| 13  | silica core–shell           | —                | antibacterial                      | [72]       |
| 14  | platinum–gold alloys        | —                | detection of disease biomarkers    | [73]       |
| 15  | CuZn bimetallic             | chemical         | enhanced bacterial inhibition      | [74]       |
| 16  | Au–Ag bimetallic            | biosynthesis     | detection of xanthine             | [76]       |
| 17  | CuFe bimetallic             | chemical         | antimicrobial                     | [78]       |
| 18  | Au–Ag bimetallic            | —                | antimicrobial                      | [78]       |
| 19  | copper and nickel bimetallic| chemical         | —                                  | [79]       |
| 20  | Au–Ag bimetallic            | biosynthesis     | —                                  | [80]       |
| 21  | Pt–Pd bimetallic            | —                | —                                  | [81]       |
| 22  | Cu Ni and Cu Ag bimetallic  | biosynthesis     | —                                  | [82]       |
| 23  | copper–silver bimetallic    | biosynthesis     | —                                  | [83]       |
| 24  | zero-valent iron/Cu          | —                | —                                  | [84]       |
| 25  | Cu@Pt core–shell            | —                | antimicrobial                      | [85]       |
| 26  | Au–Pd core–shell            | —                | —                                  | [86]       |
| 27  | Au–Ag bimetallic            | —                | —                                  | [87]       |
| 28  | Pt–Au bimetallic            | —                | —                                  | [88]       |
| 29  | zinc oxide/silver bimetallic| —                | —                                  | [89]       |
| 30  | gold-coated iron oxide      | —                | —                                  | [90]       |
| 31  | Ag@Pd core–shell            | biosynthesis     | —                                  | [91]       |
| 32  | manganese ferrite core–shell| chemical         | —                                  | [92]       |
| 33  | Cu–Ni bimetallic            | —                | —                                  | [93]       |
| 34  | core–shell Fe3O4–Au          | —                | —                                  | [94]       |
| 35  | Fe3O4@SiO2@Ag triple core–shell | chemical   | —                                  | [95]       |
| 36  | Fe3O4@Ag                    | —                | —                                  | [96]       |

Methods can improve human and environment health by helping in developing green technology and economic growth.

6 Acknowledgment

The authors acknowledge Kerman, Bam University of Medical Sciences and National Institute for Medical Research Development (NIMAD) (grant no. 963543) for their support.

References

1. Mortazavi, S.M., Khatahi, M., Sharifi, I., et al.: ‘Bacterial biosynthesis of gold nanoparticles using salmonella enterica subsp. enterica serovar typhi isolated from blood and stool specimens of patients’, J. Cluster Sci., 2017, 28, (5), pp. 2997–3007.
2. Beitolia, H., Garkani Nejad, F., Tajik, S., et al.: ‘Voltammetric determination of antimalarial by graphite screen printed electrode modified with a copper oxide nanoparticles’, Int. J. Nano Dimens., 2017, 8, (3), pp. 197–205.
3. Jahan, S., Beitoliahi, H.: ‘Carbon paste electrode modified with TiO2/Fe3O4/Mwcnt nanocomposite and ionic liquids as a voltammetric sensor for sensitive ascorbic acid and tryptophan detection’, Anal. Bioanal. Electrochem., 2016, 8, (2), pp. 158–168.
4. Jahan, S., Khorasani-Motlagh, M., Noroozifar, M., ‘DNA extraction of europium(III) complex containing 2,2'-bipyridine and its antimicrobial activity’, J. Biomed. Struct. Dyn., 2016, 34 (3), pp. 612–624.
5. Nirooand, S., Khorasani-Motlagh, M., Noroozifar, M., et al.: ‘Photochemical and DFT studies on DNA-binding ability and antibacterial activity of lanthanum(III)-phenanthroline complex’, J. Mol. Struct., 2017, 1130, pp. 940–950.
6. Khorasani-Motlagh, M., Noroozifar, M., Jahan, S.: ‘Preparation and characterization of nano-sized magnetic particles Laco03 by ultrasonic-assisted coprecipitation method’, Synth. React. Inorg. Metal-Organ. Nano-Metal Chem., 2015, 45, (10), pp. 1591–1597.
7. Moghaddam, H.M., Beitoliahi, H., Tajik, S., et al.: ‘Voltammetric determination of droxidopa in the presence of carbipoda using a nanostructured base electrochemical sensor’, Russ. J. Electrochem., 2017, 53, (5), pp. 452–460.
8. Khan, F.U., Chen, Y., Khan, N.U., et al.: ‘Visible light inactivation of E. coli, cytotoxicity and Ros determination of biocatalytically capped gold nanoparticles’, Microb. Pathogenesis, 2017, 107, pp. 419–424.
9. Poor, M.H.S., Khatahi, M., Azizi, H., et al.: ‘Cytotoxic activity of biosynthesized Ag nanoparticles by Plantago major towards a human breast cancer cell line’, Rund. Linceti, 2017, 28, (4), pp. 693–699.
10. Khatahi, M., Amini, E., Amini, A., et al.: ‘Biosynthesis of silver nanoparticles using pine pollen and evaluation of the antibacterial efficiency’, Iran. J. Biotechnol., 2017, 18, (2), pp. 95–101.
11. Khatahi, M., Memnarpour, R., Poor, M.H.S., et al.: ‘Facile biosynthesis of silver nanoparticles using descurainia sophia and evaluation of their antibacterial and antifungal properties’, J. Cluster Sci., 2016, 27, (5), pp. 1601–1612.
12. Khatahi, M., Nejad, M.S., Safari, S., et al.: ‘Plant-mediated green synthesis of silver nanoparticles using Trifolium resupinatum seed exudate and their antifungal efficacy on Neosporosporium parum and Rhizoctonia solani’, IET Nanobiotechnol., 2016, 10, (4), pp. 237–243.
13. Khan, Z.U.H., Khan, A., Chen, Y., et al.: ‘Photo catalytic applications of gold nanoparticles synthesized by green route and electrochemical degradation of phenolic Azo dye using amspe/Gc as modified paste electrode’, J. Alloys Compd., 2017, 725, pp. 869–876.
14. Mirzaei, H., Darroudi, M.: ‘Zinc oxide nanoparticles: biological synthesis and biomedical applications’, Curr. Int., 2017, 43, (1, Part B), pp. 907–914.
15. Miri, A., Darroudi, M., Entezari, R., et al.: ‘Biosynthesis of gold nanoparticles using Prospocis farcata extract and its in vitro toxicity on colon cancer cells’, Res. Chem. Intermed., 2018, 44, (5), pp. 3169–3177.
16. Khatahi, M., Alijani, H., Sharifi, I., et al.: ‘Leishmanicidal activity of biongenic Fe3O4 nanoparticles’, Sci. Pharm., 2017, 85, (4), p. 36.
Karshizi, K., Dhanuskodi, S., Gobinath, C., et al. Synthesis and characteristics of core-shell and multishell nanoparticles: a green synthetic approach, Adv. Nat. Sci., 2017, 8 (1), p. 015002.

Pradeep, P., Ahad, M.J., Vaz-Domínguez, C., et al. Synthesis of cobalt ferrite core/metallic shell nanoparticles for the development of a specific Pna/DNA biosensor, J. Colloid Interface Sci., 2008, 321, (2), pp. 484-492.

Siddiqui, K.S., Husain, A.: ‘Green synthesis, characterization and uses of palladium/platinum nanoparticles’, Nanoscale Res. Lett., 2011, 6 (1), p. 482.

Shekh, J., Jappat, S., More, P., et al.: ‘Discosperma bulbiferum mediated synthesis of novel Au core shell Ag nanoparticles with potent antibiofilm and antileishmanial activity’, J. Nanomed. Nanotechnol., 2015, 10, (12), pp. 1015-1021.

Alarjaf, N.A., El-Tohamy, M.F.: ‘ECO-friendly synthesis of gelatin-capped bimetallic Au Ag nanoparticles for chemiluminescence detection of anticancer raloxifene hydrochloride’, Luminance, 2016, 31, (6), pp. 1194-1200.

Campbell, J.L., Arora, J., Cowell, S.F., et al.: ‘Quasi-cubic magnetite/silica core-shell nanoparticles as enhanced MiR contrast agents for cancer imaging’, PLoS ONE, 2011, 6, (7), p. e21857.
Dobrucka, R., Dlugaszewska, J.: ‘Antimicrobial activity of the biogenically synthesized monometallic and bimetallic nanoparticles’, ACS Biomater. Sci. Eng., 2017, 4, (2), pp. 647–653.

Maney, V., Singh, M.: ‘An in vitro assessment of novel chitosan/bimetallic nanoparticles as delivery vehicles for doxorubicin’, Nanomedicine, 2017, 12, (21), pp. 2625–2640.

Hu, M., Li, C., Li, X., et al.: ‘Zinc oxide/silver bimetallic nanoencapsulated in Pvp/Pcl nanoparticles for improved antibacterial activity’, Artif. Cells Nanomed. Biotechnol., 2017, pp. 1–10, doi: 10.1080/21691401.2017.1366339.

Euyvazadeh, N., Shakeri-Zadeh, A., Fekrazad, R., et al.: ‘Gold-coated magnetic nanoparticles as a nanotheranostic agent for magnetic resonance imaging and photothermal therapy of cancer’, Lasers Med. Sci., 2017, 32, (7), pp. 1449–1477.

Abdel-Fattah, W.I., Eid, M., El-Moez, S.L., et al.: ‘Synthesis of biogenic Ag@Pd core-shell nanoparticles having anti-cancer/anti-microbial functions’, Life Sci., 2017, 183, pp. 28–36.

Mohammadi, S.Z., Betoofahi, H., Hassanzadeh, M.: ‘Voltammetric determination of tryptophan using a carbon paste electrode modified with magnesium core shell nanocomposite and ionic liquids’, Anal. Bioanal. Chem., 2018, 5, (1), pp. 55–65.

Argueta-Figueroa, L., Morales-Luckie, R.A., Scougall-Vilchis, R.J., et al.: ‘Synthesis, characterization and antibacterial activity of copper, nickel and bimetallic Cu-Ni nanoparticles for potential use in dental materials’, Prog. Nat. Sci.: Mater. Int., 2014, 24, (4), pp. 321–328.

Liu, W., Zhang, Y., Gu, S., et al.: ‘Core-shell Fe3O4–Au magnetic nanoparticles based nonenzymatic ultrasensitive electrochemiluminescence immunosensor using quantum dots functionalized graphene sheet as labels’, Anal. Chim. Acta, 2013, 770, pp. 132–139.

Wang, X., Wang, M., Jiang, L., et al.: ‘Dual-functional Fe3O4@SiO2@Ag triple core-shell microparticles as an effective sers platform for adipokines detection’, Colloids Surf. A, Physicochem. Eng. Aspects, 2017, 535, pp. 24–33.

Pang, Y., Wang, C., Wang, J., et al.: ‘Fe3O4@Ag magnetic nanoparticles for microrna capture and duplex-specific nuclease signal amplification based sers detection in cancer cells’, Biomed. Bioelectro. 2016, 79, pp. 574–580.