Significance of Nanoparticles as Prophylactic and Treatment Option for Bacterial and Reverse Zoonosis

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ABSTRACT

A zoonotic disease spread spontaneously from vertebrate animals to people or from humans to vertebrate animals. Over 60% of human pathogens are zoonotic in nature. Bacteria, viruses, fungus, protozoa, parasites, and other pathogens may cause zoonosis. Climate change, urbanization, animal movement and trade, travel and tourism, vector biology, human and natural causes have all had a significant impact on the emergence, re-emergence, distribution, and patterns of zoonoses. Due to the emergence of resistant strains of zoonotic pathogens, nanotechnology can be very helpful in combating such pathogens. Nanotechnology has a wide range of applications in disease diagnostics, preventative and therapeutic fields. Nanoparticles (NPs) are well-established components of various successful targeted drug delivery systems, and the characteristic physicochemical features of several nano-formulations have demonstrated excellent bactericidal effects. Aside from its therapeutic potential, nano-vaccines and theragnostic uses of nano-formulations have received considerable interest as an alternate way of combating certain microbial pathogens. This book chapter focuses on the latest applications of nanomedicine in battling key bacterial zoonotic and reverse zoonotic illnesses, as well as their potential benefits, limits, and future possibilities for developing successful eradication tactics.

Key words: Zoonosis, nanoparticles, bacterial zoonosis, reverse zoonosis, one health.

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1. INTRODUCTION

Natural transmission of zoonotic diseases from animals to humans results in more than 60% of infectious diseases. A variety of transmission modes, including direct transmission (infected organisms, contamination of food, vector bite, direct touch with a contaminated entity), Indirect or passive transmission (fomite), can result in the transmission of zoonotic disease (O'Brien et al. 2017). The word "zoonoses" originated from the Greek word "zoon" meaning animal and "noses" meaning disease. A zoonosis can be referred to any disease or infection that can be transmitted impulsively from vertebrate animals to humans or from people to animals. As compared with "anthropozoonosis" (diseases that are transmitted from animals to people) and "zooanthroponosis" (diseases that are transmitted from people to animals), which study the main mode of pathogen transmission between animals and other people, 'zoonosis' is seen to be the most suitable (Chomel and Sun 2011). In addition, the term "amphixenoses" has been developed to characterize illnesses that may spread both ways and are kept in humans and lower vertebrate species.

The emergence and reemergence of zoonotic infectious disease is aided by socio-cultural practices like farming, hunting, and tourism, as well as growing ecological changes that favor the development of pathogenic vectors. Urbanization has also increased human contact with wildlife, which serves as a significant reservoir for zoonotic infectious diseases (Jones et al. 2013). Numerous domestic and wild animal species serve as reservoirs for newly developing and reemerging human diseases. They are brought on by diseases that come from animals or products derived from animals, such as viruses, bacteria, fungi, Rickettsia, and parasites (Pal 2005).

Although it is believed that improvements in prophylactic, diagnostic, and therapeutic measures have reduced the number of deaths from infectious diseases, rapid anthropozoonotic/zoonotic (animal to human) and zooanthroponotic/reverse zoonotic (human to other vertebrates) transmission of the pathogens and the worldwide origination of resistant pathogenic strains are casting doubt on this optimistic scenario (Prasad et al. 2021). The WHO lists the emergence of extensively drug-resistant (XDR) and multidrug-resistant (MDR) bacterial populations very among the top three challenges that public health is facing in the twenty-first century. According to the microbial populations' acquired non-susceptibility to various antimicrobial groups, the resistant pathogenic strains can be categorized and characterized as MDR, XDR, and PDR (pandrug-resistant) (Magiorakos et al. 2012). The acquisition of evolutionary mutations in various genes involved in survival and their exchange among various microbial populations are the main causes of the development of resistance. This is primarily due to the inequitable and improper use of antibiotics in humans and animals, which enforces the need for new antibiotics for their therapeutic management (Meier et al. 2022).

About 6KT out of the 9KT of total antibacterial consumption in Europe is given as growth promoters to animals, accounting for nearly 90% of all antibiotics used in veterinary applications are administered orally, exceeding the recommended effective dose range far too frequently (Cantas and Suer 2014). This may stimulate resistance development by the commensal microflora of the animal gastrointestinal tract serving as a major source of resistance genes for harmful microorganisms. Furthermore, antibiotic residues enter the intestinal flora or food chain, accelerating the development of antibiotic resistance in humans (Prasad et al. 2021).

Currently, a variety of nanoparticles have been proposed for use in medical science due to the rapid development of nanotechnology. Nanomaterials will soon be employed to treat a variety of severe or chronic ailments due to their distinctive chemical and physical features (Angeli et al. 2008). First-line zoonotic bacteria treatments have included chloramphenicol, ampicillin, and sulphamethoxazole (Tollefson et al. 1998; Arshad et al. 2021). Because of the greater toxic effects, resistance of the drug, and protracted pharmacodynamics, amphotericin B, which is frequently used to treat parasite infections, has limited

utilization (Cronenberg et al. 2021). In order to prevent the spread of zoonotic diseases, MDR and antibiotic-resistant bacterial populations have been declared to be the main public health concern (Zhou et al. 2021). Due to numerous drug resistance, a lack of oral bioavailability, reduced permeability, toxicity, and high cost, current chemotherapy cannot cure infection. Considering that virus particles are similar in size to those of bacteria, nanotechnology is beneficial in the fight against both zoonotic diseases and bacteria (Wang et al. 2021).

In this context, nanomedicine can be a useful option for developing cost-effective preventative, diagnostic, and therapeutic solutions to handle communicable diseases in the age of microbial resistance. Nanoparticles (NPs) are well-established components consisting of various successful targeted drug delivery systems, and the characteristic physicochemical features of several nano-formulations have demonstrated excellent bactericidal effects. Besides its therapeutic potential, nano-vaccines and theragnostic uses of nano-formulations have received considerable interest as an alternate way of combating certain microbial pathogens. This book chapter focuses on the latest applications of nanomedicine in battling key bacterial zoonotic and reverse zoonotic diseases, as well as their potential benefits, limits, and future possibilities for developing successful eradication tactics.

2. NANOTECHNOLOGY IN MEDICINE

Nanomedicine is a discipline of medicine that uses nanotechnology data and techniques in order to prevent and cure diseases. Nanomedicine is the use of very small size particles for diagnosis, drug delivery, sensing, or impelling in a live body as shown in Fig. 1 (Prasad et al. 2021).

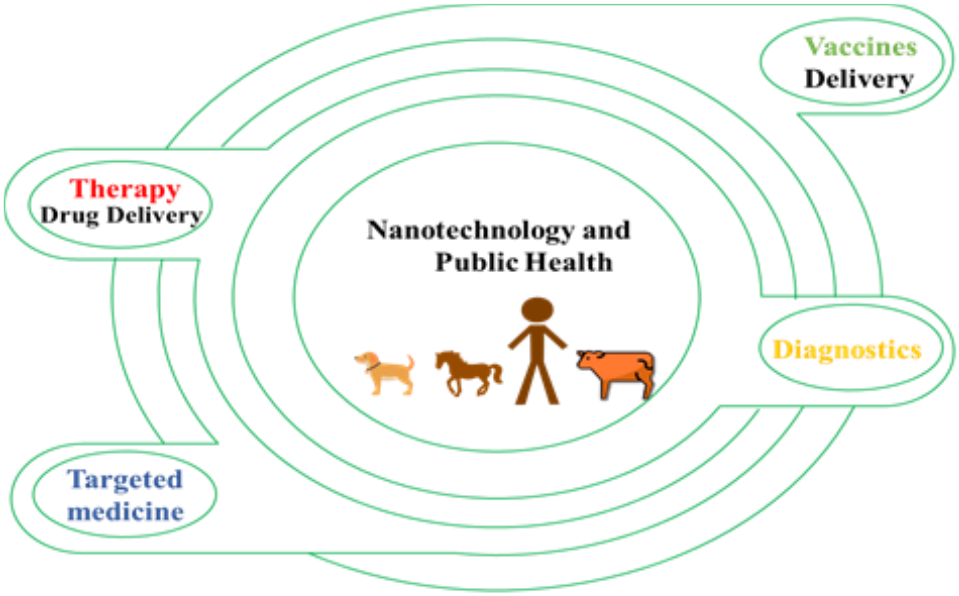

Fig. 1: Application areas of nanotechnology in public health

2.1. NANOTECHNOLOGY FOR USE IN PREVENTIVE MEDICINE

A strict preventative approach is critical for avoiding the fast spread of infectious diseases. Continuous efforts have resulted in a number of advancements in both conventional and new-generation vaccines. Various vaccines based on sub-units as well as DNA against various infectious like tuberculosis and brucellosis etc and transmissible diseases, such as the MVA85A, VPM-1002, and Vaccae TM (M. vaccae) vaccines for tuberculosis (Tameris et al. 2013), Ty21A, and Vi polysaccharide

vaccines for salmonella, Escherichia coli (E. coli) O157 vaccine for cows (Matthews 2013) "Brucella chemical vaccine" (BCV) for human and strains have been developed. However, these developments still leave room for improvement because recent sub-unit vaccines have weak immunogenicity and poor intrinsic in-vivo stability.

Additionally, these vaccines frequently face problems with limited targeting effectiveness, solubility, controlled release deficiency, fast clearance, toxic effects, and need for booster doses that must be dealt with better adjuvants and delivery of antigen through a carrier-mediated mechanism (Kim et al. 2014). Human and animal vaccines have many comparable problems, such as the necessity for protective immunity, safety, and efficient manufacture (Şenel 2021). Traditionally, many of the vaccinations approved for use on animals contain live as well as live-atrophied pathogens having antigenic activity. Subunit vaccines, which are synthesized from one or more specific components obtained from microorganisms acting as an antigen rather than a complete pathogen, are now being developed in response to safety concerns.

Adjuvants are necessary for these vaccinations to generate immunity against pathogens and prolonged safety against infections in animals. Liposomes, nanospheres, nanoemulsions, synthetic and natural polymer-based complexes, dendrimers, carbon nanoparticle-based complexes, inorganic and metal oxide nanoparticles, polypeptide nanoparticles, VLPs (Virus-Like Particles), immune-stimulating complexes (ISCOMs), and other commonly used nanocarriers for vaccine delivery have recently revolutionized the prophylactic management of several communicable diseases (Pati et al. 2018). Vaccine delivery mechanisms, such as liposomes, ISCOMs, virus-like particles, and polymeric particles, can be broadly categorized into two classes: immunostimulatory adjuvants (synthesized from microbes) that frequently show molecular patterns that are linked with pathogens and vaccine delivery systems (Singh and O'Hagan, 2003; Arca et al., 2009; Schwendener 2014).

An established framework for addressing complex needs, like M72+ AS01E, is provided by nanotechnology. It is a liposome-conjugated tuberculosis vaccine that is synthesized by the “M72’’ fusion protein and it is conjugated with the "AS01E" adjuvant complex. This enhances the antigenic ability of “M72’’ that produces a strong immune response. This ensures that it is delivered specifically to the antigen-presenting cells (macrophages and dendritic cells) (Kim et al. 2014). Vaccines are now prepared that penetrates the mucosa of animal and are applied with spray or drinking water. Mass vaccination has been evaluated in feed production, poultry, and other livestock areas. It has proven to provide adequate protection against diseases that could result in a significant financial loss on the farm and to ensure that the antigen remains stable (Scheerlinck and Greenwood, 2006; Calderon-Nieva et al. 2017).

Gregoriadis and Allison (Year) were the first to discover that liposomes can trigger immunological responses to integrated or linked antigens in the early 1970s (Allison and Gregoriadis, 1974). By altering the composition of lipids and factors required in synthesis including charge, size of distribution, catching, and where antigens or adjuvants are included, liposomes can be made to target antigen-presenting cells more effectively (Perrie et al. 2016). Due to these qualities, liposomes have received a lot of interest in the administration of vaccines against animal diseases (Sadozai and Saeidi, 2013). Using liposomes to transfer DNA complexes expressing the Toxoplasma gondii MIC3 gene of sheep was also studied. It has been demonstrated that administering a liposomal vaccination intramuscularly to sheep causes an immunological response against T. gondii (Hiszczyńska-Sawicka et al. 2012).

The immune-stimulating complexes (ISCOMs), which are also being researched for the administration of vaccines in animals, are cage-like particles with an average diameter of 40nm. These are made of Quillaja saponins, cholesterol, and phospholipids (Morein et al. 2004). ISCOMs without antigen is marketed under the brand name ISCOMATRIX and have been investigated as a possible adjuvant for vaccines (Sjölander et

al. 2001). Although the safety of these systems has been shown, it is noteworthy that there aren't many clinical investigations on ISCOMs-based vaccinations in animals, which might be explained by poor local tolerance (Sun et al. 2009; Bigaeva et al. 2016).

VLPs are non-infectious multiprotein structures that are designed to self-assemble from viral structural proteins. They range in size from 20nm to 100nm (Cimica and Galarza 2017). VLPs can be used as effective stand-alone vaccines or vaccination platforms because they have physical properties that are highly immunostimulatory, are structurally comparable to the virus from which they were produced, and have antigenic characteristics with real virions (Mohsen et al. 2017). Although their promise is not fully realized compared to human VLP vaccines there are still difficulties to be resolved with manufacturing procedures or the creation of chimeric VLPs. VLPs are increasingly being evaluated as veterinary vaccinations (Crisci et al. 2012 and Liu et al. 2012).

In the past few years, polymeric nanoparticles (PNPs) have gained a high interest due to their tiny size which gives them distinctive characteristics and behaviors (Farokhzad and Langer 2009). Controlled release, the possibility to integrate therapy and imaging, the preservation of drug molecules and their precise targeting, and the facilitation of improvements in the therapeutic index are benefits of PNPs as carriers (Crucho et al. 2017). Table I shows some recent vaccine development that is based on nanoparticles against zoonotic bacteria.

2.2. NANOTECHNOLOGY IN DIAGNOSTIC FIELD

The identification of pathogens is a crucial step in the diagnosis, effective management, and control of infectious animal diseases. When an animal come in contact with a pathogen, it may take several days, weeks, or even months until whole-organism signs indicate the existence of the disease. By then, the disease may be rampant, necessitating the eradication of whole herds (Şenel 2021). In order to diagnose infections in cattle and poultry, traditional biochemical approaches including enzyme - linked immunosorbent assays (ELISA) and plate-based techniques are being used (Vidic et al. 2017). Animal infectious illness diagnostics has also employed molecular methods like real-time PCR (RT-PCR) and polymerase chain reaction (PCR). However, the application of these techniques is not ideal for field study as they are time-consuming and usually unable to discriminate between low and highly pathogenic strains (Zarlenga and Higgins 2001; Hoffmann et al. 2009).

The inherent drawbacks of conventional diagnostic approaches, which typically rely on culture-based pathogen identification. Serological techniques, and PCR based detection techniques that are typically much time, money, and resource intensive, and are frequently overcame by nanomaterial-based platforms using laser technology, nuclear magnetic resonance (NMR), fluorescence labelling, microfluidics or lab-on-a-chip devices, flow cytometry, or biosensors for diagnosis and imaging (Tallury et al. 2010; Wang et al. 2017; Xu et al. 2018).

Gold nanoparticle (AuNP) based diagnostics have become a popular option due to their distinctive optical features, which include resonant light scattering and surface plasmon resonance (SPR) absorption. In order to help in the diagnosis, the complimentary oligonucleotide conjugated AuNPs can connect with the pathogen's target DNA to produce aggregates that change color visibly. This method of detection has been used to diagnose TB with success (Baptista et al. 2006, Soo et al. 2009). Nanocrystals called quantum dots are created from semiconductor materials. Quantum dots may be created in two ways: top-down (the dimensionality of solid matter is gradually decreased), and bottom-up (quantum dots are formed by chemical synthesis or epitaxial growth). These techniques have been successful in creating quantum dots with diameters of a few nanometers, which are sufficiently tiny to exhibit quantum mechanical features. Quantum dots (QDs) are remarkable for having very composition-and size-dependent optical and electrical characteristics (Pisanic Ii et al. 2014).

Table 1: Vaccine developed on nanoparticles against zoonotic bacteria

Sr. No.	Antigen	Nanoparticles	Bacteria	Application	Action	Model	References
1	Protective antigen (rPA) and lethal factor (rLF)	Nanoemulsion conjugation	*Bacillus anthracis*	Nasal Immunization	Start T helper 1 and 2 response	Mice	(Bielinska et al., 2007)
2	Recombinant BLSOmp31	Poloxamer 407-Chitosan (P407-Ch)	*Brucella ovis*	Intranasal	Starts IgA response	Rams	(Díaz et al. 2019)
3	*Yersinia pestis* V immunogen fused with protein anchor (V-PA)	Near-filed scanning optical microscopy (NSOM), atomic force microscopy (AFM)	*Yersinia pestis*	Intranasal mucosal vaccination	Start T helper 1 and 2 response	Mice	(Huang et al. 2014)
4	Outer membrane protein (Omp31)	Calcium phosphate, Aluminum hydroxide and chitosan NPs	*Brucella melitensis*	Subcutaneous injection	Th17 response	Mice	(Abkar et al., 2019)
5	Glycoconjugate vaccine	Gold nanoparticles (AuNPs)	*Burkholderia pseudomallei*	Intranasal	High antibody titer	Mice	(Gregory et al. 2015)
6	Clostridium perfringens ε-toxin	Membrane-camouflaged nanoparticles (MNPs) Poly (DL-lactide-co-glycolide) Carboxylate End Group (PLGA)	*C. perfringens*	Intravenous	3-day protection	Mice	(Xu et al., 2023)
7	Listeriolysin peptide 91-99 (LLO91-99), glyceraldehyde-3-phosphate dehydrogenase 1-22 peptide (GAPDH1-22)	Gold glyconanoparticles (GNP)	*Listeria monocytogenes*	Intravenous	Vaccinated mothers gave birth to new born free of bacteria	Mice	(Calderón-Gonzalez et al. 2016)

The special qualities of QDs have been used in a variety of ways during the past 15 years to create more accurate, quick, and practical bioassays. The safety of QD components, such as Cd, as well as problems with test repeatability, are of particular concern. Due to these problems, it has been suggested that QDs have been restricted to specialized investigations (Resch-Genger 2008). For the identification of Mycobacteria, *E. coli*, Salmonella, Cholera toxin, etc., the prescribed method has been effectively used (Gazouli et al. 2010; Yang and Li 2006; Goldman et al. 2004).

Numerous medicinal applications, including cancer treatment, nano diagnostics, and bioimaging, have effectively used magnetic nanoparticles (Wang et al. 2017). The increased separation and detection of aligned magnetic nanoparticles bound to targeted drugs in the presence of an applied magnetic field forms the basis for this diagnostic (Shinde et al. 2012). Iron oxide nanoparticles with magnetite or maghemite cores, which are frequently used magnetic nanoparticles, have been employed as contrast to magnetic resonance imaging. In order to identify variety of pathogens including viruses, bacteria, and parasites, the surface of iron oxide nanoparticles can typically be changed and coupled with antibodies, proteins, and nucleic acids. The effective and early detection of the infectious disease (malaria) has been proven using magnetic nanoparticles with an iron oxide core and a silver shell (Yuen and Liu 2012).

For the sensitive and reliable diagnosis of M. tuberculosis for TB, nanodevice-based diagnostic systems have been created. But for now, it's still quite difficult to quickly identify TB patients in underdeveloped nations (Liong et al. 2013). A schematic diagram showing the procedure of M. tuberculosis detection through magnetic barcode assay is shown in Fig. 2. This ligand attached magnetic NP-based probes have

been used to specifically identify a variety of pathogens, including Mycobacteria, Listeria, Staphylococcus, E. coli, and others, to the single cell level (Prasad et al. 2021).

For the detection of different infections, silver nanoparticles, metallic nanowires, Detonation Nanodiamond (DND) Detection Systems, silica nanoparticles, etc. are also utilized; nevertheless, the majority of these revolutionary nano diagnostics are too expensive for widespread usage, especially in developing countries (Tallury et al. 2010; Soo et al. 2012). Table 2 lists the numerous zoonotic and reverse zoonotic bacterial illnesses for which nano-diagnostic uses have been reported.

2.3. NANOTECHNOLOGY FOR USE IN THERAPEUTICS

Currently, drug delivery systems dominate nanomedicine, making up more than 75% of all sales (Wagner et al. 2006). The size range of nanomaterials is comparable to that of proteins and other macromolecular structures found inside live cells. As a result, nanoparticles are prepared to use the cellular machinery already in place to assist the transport of pharmaceuticals. The special properties of nanoparticles (NPs) that include medications are encapsulated, disseminated, absorbed, or conjugated which might improve performance in a range of dosage forms. When properly designed, drug particles can have greater adherence to biological surfaces, higher saturation solubility, quick dissolution, and resistance to settling, all of which contribute to a faster beginning of therapeutic action and higher bioavailability. Furthermore, the bulk of molecules inside a nanostructure are found on the particle surface, maximizing the loading and delivery of cargoes including medicines, proteins, and polynucleotides to selected cells and tissues (Bamrungsap et al. 2012).

Nano formulations are proven bactericidal agents that can be used alone or in conjunction with current antibiotics to treat microbiological diseases. These properties have been skillfully exploited in nanotherapeutics to avoid drug resistance and microbes that produce biofilms (Razei et al. 2017). In order to create nanotherapeutic approaches against microbial superbugs, a wide range of metallic or bimetallic nanomaterials, including iron oxide (Fe3O4), zinc oxide (ZnO), titanium oxide (TiO) NPs, gold and silver NPs, or their combination in a single NP, are widely used (Kulshreshtha 2017; Baptista 2018). In addition to acting as a direct bactericidal agent, nanocarriers offer excellent therapeutic control through targeted delivery of existing antibiotics to the infection sites and sustained drug release to maintain the minimum inhibitory concentration (MIC) for an extended period of time while minimizing potential side effects (Bermudez et al. 2017). This may also help shorten the duration of certain intracellular, antibiotic-resistant microorganisms treatment regimens, such Mycobacteria (Xu et al. 2018).

A variety of nanoforms, including solid metal-containing NPs and polymers as well as biological materials including albumin, gelatin, and phospholipids for liposomes, have been tested as drug delivery systems. High size variation polymer-drug conjugates are often not regarded as NPs. However, they are also included into these nano delivery systems since their size can still be adjusted to within 100nm. These nano delivery systems can be made to have medications dissolved inside the particle matrix, encapsulated inside lipids, or absorbed onto the particle surface. In addition, the increased permeability and retention (EPR) effect allows nanoparticles to aggregate preferentially at tumor, inflammatory, and infectious sites. The EPR effect involves site-specific properties that are not connected to healthy tissues or organs, leading to more precise targeting (Bamrungsap et al. 2012).

2.4. NANOTECHNOLOGY FOR TREATMENT OF BACTERIAL AND REVERSE ZOONOSES

Infectious diseases, particularly bacterial diseases, are huge burden on public health, killing about 14 million people each year (Nii-Trebi 2017; Ali et al. 2017). Bacterial infections molecular components, such as their genetic material, ribosomes, cell membranes, cell wall, and biosynthetic pathways, differ greatly

Table 2: Some recent nano diagnostic tools for detection of zoonotic bacteria

Sr. No.	Detection technique	Nanoparticle	Pathogen	Application	Model	Reference
1	Magnetic bead-based DNA detection assay	QDs associated through biotin–streptavidin conjugate	*E. coli* O157:H7	might be used for quick illness diagnosis	*In-vitro*	(Liu et al. 2008)
2	Surface-Enhanced Raman Scattering (SERS)	Nano silver associates	*E.coli*	Helpful in pathogen detection	*In-vitro*	(Zeiri and Efrima, 2006)
3	Genus-specific anti-lipopolysaccharide (LPS) monoclonal antibody (mAb)	Gold nanoparticle	*Salmonella* spp.	Novel competitive strip sensor for fast detection	*In-vitro*	(Wang et al., 2016)
4	Bio-barcoded electrochemical biosensor	Gold nanoparticles (AuNPs), magnetic nanoparticles (MNPs)	*B. anthracis*	Potential applications in multiple detection of bioterrorism threat agents	*In-vitro*	(Zhang et al., 2010)
5	Aptamer	Fe3O4@Au magnetic nanoparticles	*S. aureus*	High specificity can be achieved within 50 min	*In-vitro*	(Pang et al., 2019)
6	Magnetic separation and lateral flow immunoassay (LFIA)	Fe3O4	*L. monocytogenes*	Low cost, good selectivity and convenience	*In-vitro*	(Du et al., 2022)
7	Loop-mediated isothermal amplification (m-LAMP) amplicons	Colloidal gold solution	*Leptospira*	Fast detection	Urine	(Bamrungsap et al., 2012)

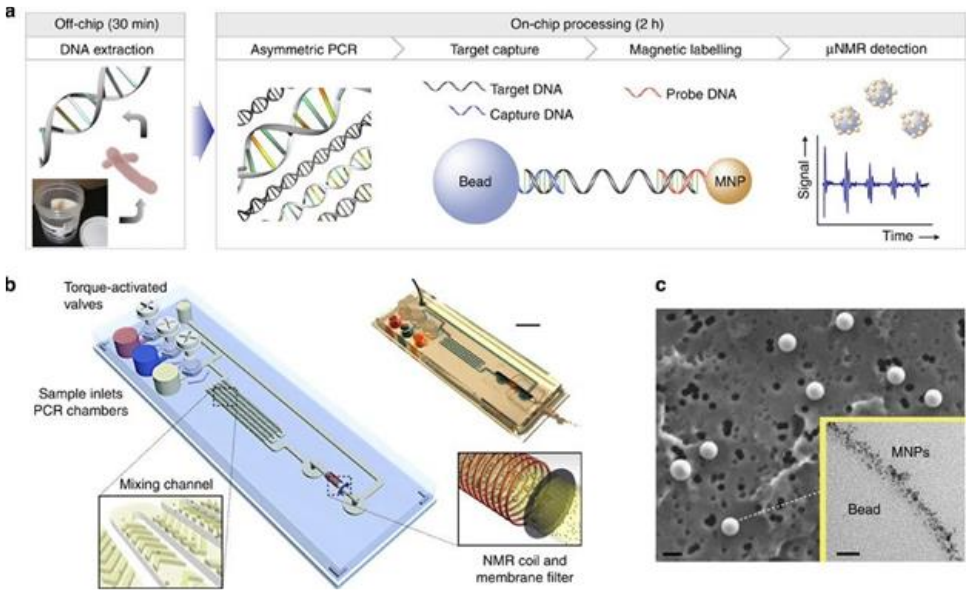

Fig. 2: Magnetic barcode assay: Amplified isolated DNA is labbled with MNPs beads and varifiation is done under electron microscope (Liong et al. 2013)

from human cells, these elements are typically used to develop antimicrobial drugs (Ganewatta and Tang 2015). Efflux pumps, enzymatic suppression by hydrolytic degradation or chemical alterations like the addition of a phosphate group, acetylation, hydrolysis, changing target, reprogramming biological synthesis, and accelerated evolution of acquired resistance in microorganisms are some of the methods

used by bacteria to resist antimicrobials (Van et al. 2018). Furthermore, several antibiotics, including fluoroquinolone and aminoglycosides, have detrimental side effects (Poulikakos and Falagas 2013). The majority of multidrug resistance (MDR) infections need extended antibiotic therapy that are accompanied by significant health-care costs (Masri et al. 2019). Some recent nano antibiotics have been listed in Table 3.

Several of the most common infectious diseases are bacterial in origin and have the potential to spread through zoonotic and reverse zoonotic mechanisms, including tuberculosis, salmonellosis, shigellosis, pneumococcal disease, campylobacteriosis, listeriosis, and E. coli infection. These diseases pose a serious risk to the health of both humans and animals worldwide (Cassini et al. 2018). The rapid development of antibiotic resistance among these microbial groups is also posing a significant threat, as evidenced by the fact that Salmonellae and Staphylococcus aureus were designated as high priority bacterial pathogens that cause disease in the first report by the WHO on high priority list of resistance bacteria while Enterobacteriaceae group bacteria were documented as critical (Zaragoza-Bastida et al. 2020).

With the conjugation of oral amikacin administration and lipid-crystal NP delivery method, MatinasBioPharma (MTNB) has disclosed significant preclinical effectiveness of MAT2501 in the in-vitro model of Mycobacterium abscesses infection (Da-Silva et al. 2012). Since liposomal NP core has a large drug loading capacity, it is possible to prevent hydrophilic antimicrobial medicines from being degraded in-vivo by encasing them within the liposomal NP core. Aerosolized liposomal antibiotics (ciprofloxacin, tobramycin, amphotericin B, and amikacin) have been shown to have a considerable curative impact in the prevention and treatment of acute and chronic respiratory tract infections (Bassetti 2020).

Combining AgNPs with Simvastatin led to a synergistic impact of bactericidal antibacterial activity against a number of resistant species, including extended spectrum beta lactamase producing E. coli and methicillin resistant S. aureus (Figueiredo et al. 2019). Silver nanoparticles due to their antibacterial qualities, are also applied in the medical industry to treat skin wounds and dermatitis (Owusu et al. 2016). Since S. aureus and K. pneumoniae have been shown to be efficiently controlled by Cryson nano sliver antibacterial and deodorant agent, it may be useful to manage bacterial zoonoses. A copper oxide-nanorod-based artificial enzyme called "NanoZymes" has been shown to fight against E. coli and Golden Staph infections by photo modulated reactive oxygen species formation, which is efficient in controlling nosocomial and aerosol infections (Jansson et al. 2014). The development of novel nano-antimicrobials using a wide range of molecules against numerous resistant and biofilm-producing microbes is ongoing, but them in-vivo efficacy, toxicity, cost effectiveness, and economic viability need to be properly assessed before common applications of these formulations can be made for greater public health benefit (Hadad et al. 1995).

3. CONCLUSION

The scientific field of nanotechnology works with particles with a size range of a few nanometers. According to the article, nanotechnology has uses in the detection, diagnosis, and management of industries, including pharmaceuticals, health sciences, and livestock etc. The creation of nanoparticles involves different metals, including nickel, gold, silver, and casein micelles etc. Nanotechnology also makes it feasible to administer drugs. Past predictions of nanomedicine as a cure-all have generated more enthusiasm than reality, and the underlying difficulties are frequently disregarded until they are suddenly noticed during clinical translation. The potential for nanomedicine is unquestionably great, but the understanding of how these nano-formulations behave in-vivo for therapeutic use is limited. These problems are now being addressed more precisely for practical application and are anticipated to produce more practical answers soon.

Table 3: Recent nano antibiotics against zoonotic bacteria

Sr. No.	Nano antibiotic	Deliver system	Pathogen	Action	Model	Reference
1	AgNP with Colistin, penicillin G and Amoxicillin	Adjuvants	*Salmonella enterica, Staphylococcus aureus, Escherichia coli, Actinobacillus pleuropneumoniae, Streptococcus uberis, Pasteurella multocida*	Antibacterial actions against resistant strains	*In-vitro*	(Smekalova et al. 2016)
2	Gentamicin-loaded magnetite block ionomer complexes (MBICs)	Magnetite block ionomer complexes	*B. melitensis*	High clearance of pathogen	*In-vitro*	(Jain-Gupta et al. 2013)
3	Doxycycline hydrochloride and rifampicin	Polymeric nanoparticles	*B. abortus*	Effective	*In-vitro* and mice	(Dawre et al. 2022)
4	Zinc oxide nanoparticles (ZnO-NPs), copper oxide nanoparticles (CuO-NPs)	Food borne zoonosis control	*L. monocytogenes*	Effective antibiotic action	*In-vitro*	(Osaili et al. 2019)
5	Rifabutin	Encapsulated in liposomes	*Tuberculosis*	Increased therapeutic activity	Rat	(Gaspar et al. 2008)
6	Iron oxide nanoparticles (α-Fe2O3)	Anti-bacterial	*Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumonia, and Escherichia coli*	Strong Antibiotic activity	*In-vitro*	(Buarki et al., 2022)
7	Metal-based dendrimeric nanoclusters with isoniazid	Dendrimer complexed with copper	*M. tuberculosis*	Alternative and an innovative therapy in the treatment of tuberculosis	*In-vitro*	(Rodrigues and Shende, 2020)

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