



Nanonephrology in Veterinary Medicine: A Branch of Nanomedicine for Renal Diseases in Animals

E.K AL-Hamdany* and Thanoon Y. Al-hbiti

Department of veterinary pathology and poultry Diseases, college of veterinary medicine, University of Mosul, Mosul, Iraq.

*Corresponding Author, Entisar K. AL-Hamdany, E-Mail: ekalzory@uomosul.edu.iq

ABSTRACT

Nanotechnology is a fast-growing technology because of its capability of solving many problems related to animal production and health and plays important roles in the veterinary medicine field. Nanoparticles are characterized by minimal size, it has a role in the improvement of drug delivery, animal health and production. Also used as alternative antimicrobial agents instead of using large amounts of antibiotics, new drug and vaccine as delivery agents with improved characteristics and performance, diagnostic therapeutic, nutrient delivery, feed additive, biocidal agents and increase the quality of food by using many kinds of nanoparticles such as polymeric nanoparticles, liposomes, dendrimers and metal nanoparticles. Nanonephrology is a branch of nanomedicine that deals with the study of kidney proteins at the nano level and study of cellular structure and process that happened in the kidney with the help of imaging by nano technique and with use of very little size (nano size) particles in treatment of kidney disorders which include acute and chronic kidney disease. With the help of nanotechnology, we replace kidney transplantations and dialysis with low cost and safe animal and human life. Nanonephrology gives us information of molecular structure at the cellular level in normal kidney functions and at pathological state by studying the chemical and physical characteristics of kidney proteins and cells at the atomic level by design and structure of nanoparticles that will be matched to the renal cells thus safely and easily perform their function in the kidney. The advantages of nanonephrology in nanomedicine are focused on renal nano diagnostics for studies of basic renal function and early diagnosis of acute and chronic kidney disorders.

Keywords: kidney disease, Nanomedicine, Nanonephrology, *J. Appl. Vet. Sci.*, 5 (4): 17 -24. Nanoparticles .

Original Article:

DOI: <https://dx.doi.org/10.21608/javs.2020.117996>

Received :30 July, 2020.

Accepted :24 Aug., 2020.

Published in October, 2020.

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INTRODUCTION

Nanotechnology is a fast-moving technique originally developed around 1974 for the assembly of novel materials ranging from (1 to 100 nm) derived from the Latin word (nanus), which means very small in scale. (Underwood and VanEps, 2012; Manuja *et al.*, 2012; Saha *et al.*, 2011), it's developed at atomic, molecular and macromolecular levels, it's most important technologies of the 21st century, and it's creating new probe devices and materials which has a wide range of application in medicine and veterinary medicine (Underwood and VanEps, 2012; Muthu *et al.*, 2014; Hassanzadeh *et al.*, 2018).

This technology takes an interest in numerous fields including agriculture, science and infection treatment and it has potential impacts for applications and researchers (Hill and Li, 2017; Hassanzadeh *et al.*, 2017; Tassew Belete Bahru and Eyasu Gebrie Ajebe, 2019).

The application of nanotechnology in veterinary medicine is important in many branches of animal disease treatment (Fattal, 1989; Hong Ying Mao *et al.*, 2013). Nanonephrology is the branch of nanotechnology and nanomedicine that deals with the study of kidney disorders (acute and chronic disease) at the atomic and cellular level, study kidney protein structure and treatment of the kidney diseases by nanoparticles which designed for kidney cells (Medina-

Reyes et al., 2017; Allen et al., 2005; Farokhzad and Langer,2009; Num and Useh,2013), creation and use of materials and devices that used for diagnosis and therapy of renal disease at molecular and atomic levels (**Patil et al., 2009; Bhaskar et al.,2010; Williams et al.,2016**). This will play the role treatment of patients with kidney disease in the future. (**Lee et al., 2015; Garabed Eknayan, 2017; Vaidya et al.,2010**).

The positive impact of nanotechnology in nephrology is based on the development of renal nano diagnostics for basic renal function studies, the early diagnosis of acute and chronic kidney injury and improvement of magnetic resonance imaging while the disadvantage of nephrology is the renal clearance of nanoparticles (**Nazila et al., 2016; Singh et al., 2011; Mahrukh and Kianoush,2017**).

Application of Nanotechnology in Veterinary Medicine

Uses of nanotechnology in the veterinary field have a signification effect in numerous fields includes therapeutics, tissue building, diagnostics, immunization and disinfectants (**El. Sayed and Kamel, 2018; Saini et al.; 2010; Chen et al.,2016; Rajendran,2013**). The uses of nanotechnology in animal production include Vitamins, probiotics, executives of drug, untraditional supplement, detection and removed of causes of infection without surgery and similarly (**Lee et al., 2015, Pisignano, 2007; Peer,2007; Erathodiyi and Ying,2011**).

The creation of new synthetic molecular nanoparticles can help in the treatment of pet's disease population and protect them from viral, bacterial infection and accelerate wound healing (**Rai et al., 2009; Mishra,2010; Meena et al. 2018**), for examples feline hyperthyroidism is the common endocrine disorder affect cat so, Nanomedicine used to treat this disorder by manipulating the level of thyroxin 3 (T3) and thyroxin (T4) in the blood by maintaining of secretion of the required level of drug thiamazole at the level which body needs. (**Longson, 2007; Chakravarti and Balaji, 2010**). Also using of normal antibiotics in animal production can leave a residue that affects the consumer (Human) while using of nanotechnology reduces the amount of antibiotics because of their small size (Nano size) (**Longson 2007, Narducci, 2007; Yu et al.,2010; Wang et al., 2011**)

Role of nanomaterials in Animals Health and Nutrition

Because of nanomaterials are in extensive, act as growth-promoting agent, utilized in low quantities and good immune-stimulating agent so, it produces many benefits for animal feed production, they also manipulate feed pathogens and enhance fragmentation processes in rumen of animals (**Swain et al., 2015; Zha et al.; 2007; Zadeh and Moradi-kor,2013**). One

of the most common Nanomaterials used in veterinary medicine is zinc oxide to improve growth rate, disorders affected livestock reproduction and to enhance immune response; diarrhea may be a side effect of using zinc oxide also decrease of somatic cell count in cows with subclinical mastitis (**Bollo, 2007; Sanker et al., 2018; Thulasi et al.,2013; Rajendran et al.,2013; Scott,2005**).

Silver nanoparticles are used in pet animal care as disinfectants by mixed with shampoos for topical use (**El-Sayed and Kamel, 2018; Ding Ping et al., 2018; Riley and Vermerris,2017**). Further application of nanotechnology in veterinary medicine is to raise the bio viability of nutrients and enhancement of growth rate and performance also many nanomaterials may be used with combination with hydrogels or zeolites to enhance the water excellent (**Hill et al., 2017; Tang et al., 2019; Fengue, 2003; Mieszwska et al.,2013**). Nanoparticles have an effect on sperm purification, so nanoparticle used to potentiate fertilization efficiency that in part facilitates fertilization of mono females from one collection (**Medina- Reyes, 2017; Underwood and VanEps, 2012, Dilnawaz et al., 2015**).

Nanonephrology

It is a nanotechnology nanomedicine come from Greek word (Nephros) that deals with the study of all cellular processes happened in kidney and protein present in the kidney at a nano-level with the use of nano-sized particles as nanomedicines in treatment of many kidney diseases (**Pisignano, 2007; Lee et al., 2015**).

Nanotechnology is a new technology that contributing to the development of Nephrology and study the different pathological condition that directly or indirectly affects the kidney function like diabetes, hypertension and autoimmune disease, so in future nanoparticle will play an important role in the treatment of patients with severe kidney disorders (**Soriano et al.,2018; Rayan et al.,2016; Jain et al.,2011**).

Nano nephrology will give all information about cells that involved in the function of the kidney at the pathological level (**Pisignano, 2007; Liu et al.,2013**). Nanoparticles in nephrology used as biomarkers in imaging technology so that many types of biomarker will be used in nephrology because the presence of these markers in blood and finally go to the kidney, filtered and excreted out of the body through urination and these biomarkers can be detected in urine by Eliza technique (**Lee et al., 2013; Bollo, 2007**).

Urine is common most suitable body fluid and can be easily collected so used for detecting changes of the pathophysiology of kidney disease; it is directly

filtrated by kidneys and containing many soluble biomarker proteins, ELISA is the main clinical approach for the sensitive measurement of protein biomarkers in urine and is applied in clinical laboratories for clinical markers measurement for detection of urinary system disorders (Despina *et al.*,2016; Rizzo *et al.*,2013).

Using of nanoparticles in nephrology to filter and purify the blood passing through the kidney and thus eliminate the need of kidney dialysis that is very expensive and very painful, so using of nanofiber are more useful and efficient compared with dialysis (Bayan *et al.*, 2016; Rajiv Saini *et al.*, 2012). Nanofiber used in the treatment of kidney disorders is much cheaper and not electric dependent than other techniques like dialysis (Rayan *et al.* ,2016). Development of human nephron filter (HNF) is a new invention in Nano nephrology field applied to the human who is suffering from renal failure, and this invention will replace the need to kidney transplant and dialysis (Soriano *et al.*, 2018, Lee *et al.*, 2015; Sereemaspann *et al.*,2008).

Nanomedicine and nanoparticles for Animals renal diseases

Nanomedicines have a great interest for the diagnosis, treatment, and research of disease including renal diseases., nowadays Nanotechnology involves the engineering of molecules and atoms at the submicron level and delivery of drugs to specific tissues target (Wu *et al.*,2018; Pawar and Kaul,2012). Nanomedicines in the clinic have reduced off-target side effects, increased solubility of drugs and provided diagnostic tools(Thomsen *et al.*, 2013). Possible applications of nanotechnology in medical science as Therapeutic indication, Preventive indications and Diagnostic indications, there is an increase of Nanomaterials that may have particular implications for kidney diseases(Nazila *et al.*,2016). Organic or Inorganic nanocarriers, which refer to as nanoparticles, can be engineered to imaging agents or deliver drugs with unique characteristics. For example, nanoparticles delivery improves biodistribution and pharmacokinetics and enables targeted delivery of drugs to specific tissues, subcellular compartments or cells(Williams *et al.*,2016).

Nanoparticles can have either hollow aqueous or a solid core biodegradable, degradable and bio eliminable structures generally <150 nm in size as shown in Fig.1 (Nazila *et al.*,2016). The surface layer of these particles coated with inert polymers, these particles can shield from blood components. Polyethylene glycol, which is a type of polyethers, has been mostly used for this purpose. Surface layers core of the nanoparticles can be incorporated with a variety of payloads: hydrophobic or hydrophilic,

proteins,small-molecule drugs, nucleic acids, peptides, or imaging agents(Houshang *et al.*,2013; Williams *et al.*,2016; Fady *et al.*,2019).

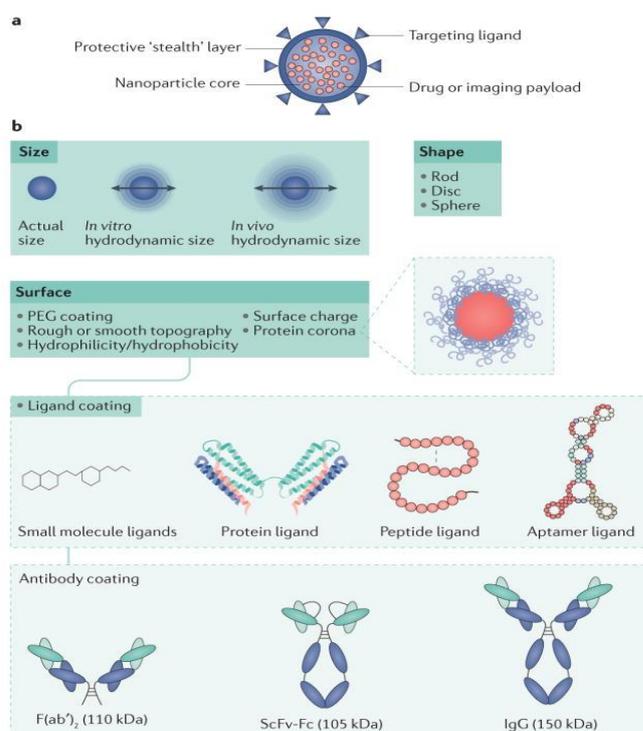


Fig.1: Nanoparticle composition and features (Nazila *et al.*,2016)

Clearance of Nanoparticle from Kidney

The absence of renal clearance and biodegradation of nanoparticles is considering a downside of Nanomaterials, as we know nanoparticles, as we know nanoparticles used in diagnostic and therapeutic purposes so, it can accumulate in the body tissue as many of them contain heavy metals on fluorescent agents (Choi *et al.*,2007, Patil,2009; McBainet *et al.*,2008). The renal clearance of nanoparticle depends on many factors like Shape, nature, hydroxylamine size, crystallinity, stability and surface activity (Lee *et al.*, 2015; Buzza *et al.*,2007; Otto,2015), so the coating of nephrotoxic drugs like anti-inflammatory agents and chemotherapeutic agents prevent kidney damage (Garabed, Ekuoyan, 2017; Faisal *et al.* ,2007; Williams *et al.*,2015). If the hydrodynamic diameter of nanoparticles is less than (5-15nm) renal clearance is acceptable for examples after injection of quantum dots intravenously these particles with a small hydrodynamic diameter (4.36 nm) are cleared within 48 while those of (8.65 nm) diameter ham a half-life of clearance about (20 hours) (Bentolila,2009; Michalet *et al.*,2005; Xu *et al.*,2017)

Mechanism of Elimination of Nanoparticle from Kidney

There are two mechanisms of eliminations of nanoparticles from the kidney: the direct one it's by glomerular filtration of these particles from kidney

tubular and the indirect mechanism elimination by biodegradation products(Kim *et al.*,2006; Ovidiu and marcel,2013; Nuray *et al.* ,2016). A second route of elimination through the liver which is designated to capture and eliminate nanoparticle of (10-20 um) of hydrodynamic diameter like viruses but this consider a slower route (Rahimnejad *et al.*,2006; Sirirat *et al.*,2013; Tang *et al.*, 2019; Raddy and Couvreur, 2011).

Study of Renal Function by Using Nano nephrology and Nano diagnostic of Kidney Diseases

Nano nephrology is an extension of nanomedicine with investigation of kidney processes at a cellular level. (Lee *et al.*,2015; Kukowska-latallo *et al.*,2005; Elgqvist,2018), recently using of nanotechnology in nephrology is to improve diagnosis of renal disease if normal epithelium is damaged by Ischemia or toxic agents, apoptosis, necrosis and cell death all there will be studies by using of nanotechnology and nano nephrology, and this indicated by a marked increase in blood urea and serum creatinine which means tissue damage (Rajiv Saini *et al.*, 2012; Lee *et al.*, 2015).

If the normal epithelium damage by Ischemia or toxic agents, there are two diagnostic methods for early indication of this damage the multiple marker strategy by using fluorimetric treatment system based on the combination of nanotechnology and microfluidics which depends on measuring the relative ratio of some biomarkers in urine, a second strategy is by detection lipocalin with neutrophil-gelatinase which is an early biomarker for acute renal failure which represents a significant disorder in clinical nephrology in a wide range of different disease processes Fig.2 (Vaidya *et al.*,2010; Li *et al.*,2015).

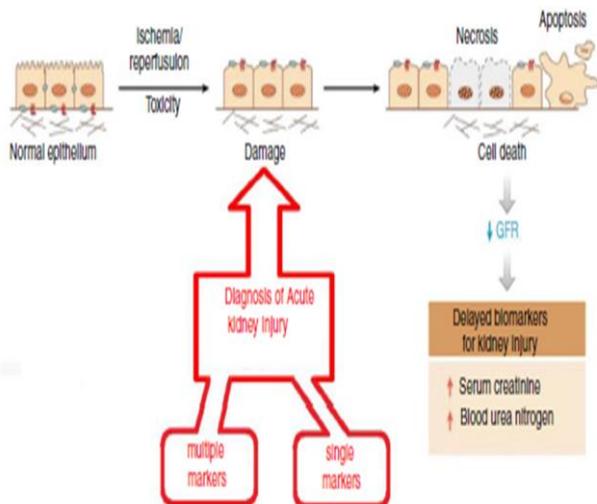


Fig. 2: Time of application of two types of nano markers for early diagnosis (Vaidy *et al.* ,2010).

While the measurement of markers in blood does detection chronic renal disease, this diagnosis is based on the fact that renal failure changes the percentage of more than40 volatile organic compounds this is done by using of carbon-coated nanotubes as in the instrument called “electronic nose”, which is act as a sensor, it is available commercially(Haick *et al.*,2009; Soriano *et al.*,2018).

Nano regeneration of renal tissue

Nanotechnological structure supports (scaffolds) of different types: inorganic (e.g. mesoporous silica or quantum dots,)organic (e.g. nanocellulose, carbon nanotubes, and derivatives) and biological (e.g. use of clean renal tissue) is used for tissue and cellular Nano regeneration (Williams *et al.*,2016).The advantages of support scaffolds are: reproduces the extracellular native matrix, high cell compatibility, improves the properties of the conventional microstructured supports and promotes cell proliferation and adhesion (Guerrero *et al.*,2017). the growth of endothelial cells of the glomeruli capillaries is an example by using of fluorescence microscopy showed proliferation of endothelial cell during five days in nanostructured supports compared with conventional Fig.3 (Zhang and Webster,2009).

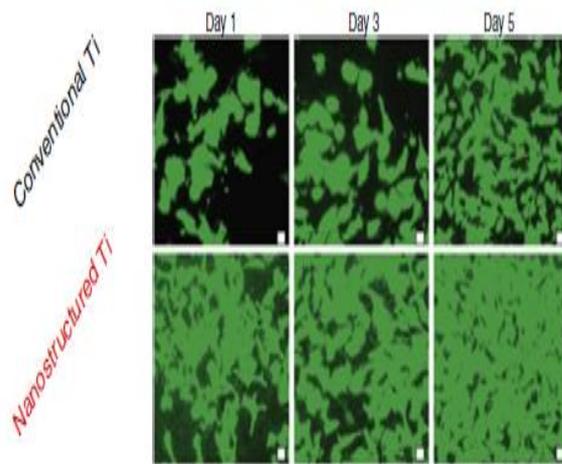


Fig.3: Comparison of growth of endothelial cells in nanostructured supports and conventional one(Zhang and Webster, 2009)

CONCLUSIONS

It has been concluded that nanotechnology and nano nephrology is a newly discovered technique, in which nanomaterials and nanoparticle used to purify and filter blood that passes through the kidney and there is no need to kidney dialysis that is very painful and coasted. This technique contributed to solving several problems in animal health and production, and it's contributing to diagnosis, immunization, tissue building and disinfection. The nanotechnology in nephrology improved the old technique, discover and provide new tools and facilitated the discovery and

treatment of renal disorder with a fast time and low cost. In conclusion, Nano nephrology is still nanotechnology capable of improving therapies, diagnostic, renal teragnosis and promoting the study of renal function. It will be suggested that in the future we need to study toxic and pathologic effects of nanoparticles in other organs like liver, brain and heart. Therapeutics and molecular diagnostics should be combined with nanotechnology to improving diagnosis and treatment of all animal diseases.

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How to cite this article:

E.K AL-Hamdan and Thanoon Y. Al-hbiti .2020. Nanonephrology in Veterinary Medicine: A Branch of Nanomedicine For Renal Diseases in Animals. *Journal of Applied Veterinary Sciences*, 5(4): 17 - 24.
<https://dx.doi.org/10.21608/javs.2020.117996>