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NANOTECHNOLOGY AND ITS APPLICATIONS IN MEDICINE AND COVID-19.

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Abstract

In the Nanotechnology nanomaterials are the leading edge of the rapidly developing field. The small size of nanomaterials makes it indispensable & superior in many human activities. Nanotechnology offers multiple benefits like site-specific & target oriented delivery in treatment of chronic human diseases. The current review represents an updated summary of recent advances in the field of Nano medicines & Nano based drug delivery systems. Nanomaterials are useful to improve efficacy of both novel & old drugs. Nanotechnology based drug delivery system have also applications in viral infections. The emergence of severe acute respiratory syndrome coronavirus 2(SARS-CoV2) soon lead to the global pandemic. Smart Nano carriers have accelerated the design of several therapeutic, prophylactic & vaccine development against COVID-19.

Keywords

Nanoparticles, SARS-CoV2, Nanomaterials, Diagnosis, Drug delivery.

Nanotechnology

Nanotechnology is the study of extremely small structure having size of 0.1-100 nm. Nanotechnology is the treatment of individual atoms molecule or compounds into structure to produce materials and devices with special properties . The pharmaceutical involves two types of work from manufacturing of nanomaterials

1.Top down :- Size of large structure reduce to smallest structures.

2.Bottom up :- Changing molecules and atoms into Nano- structure.

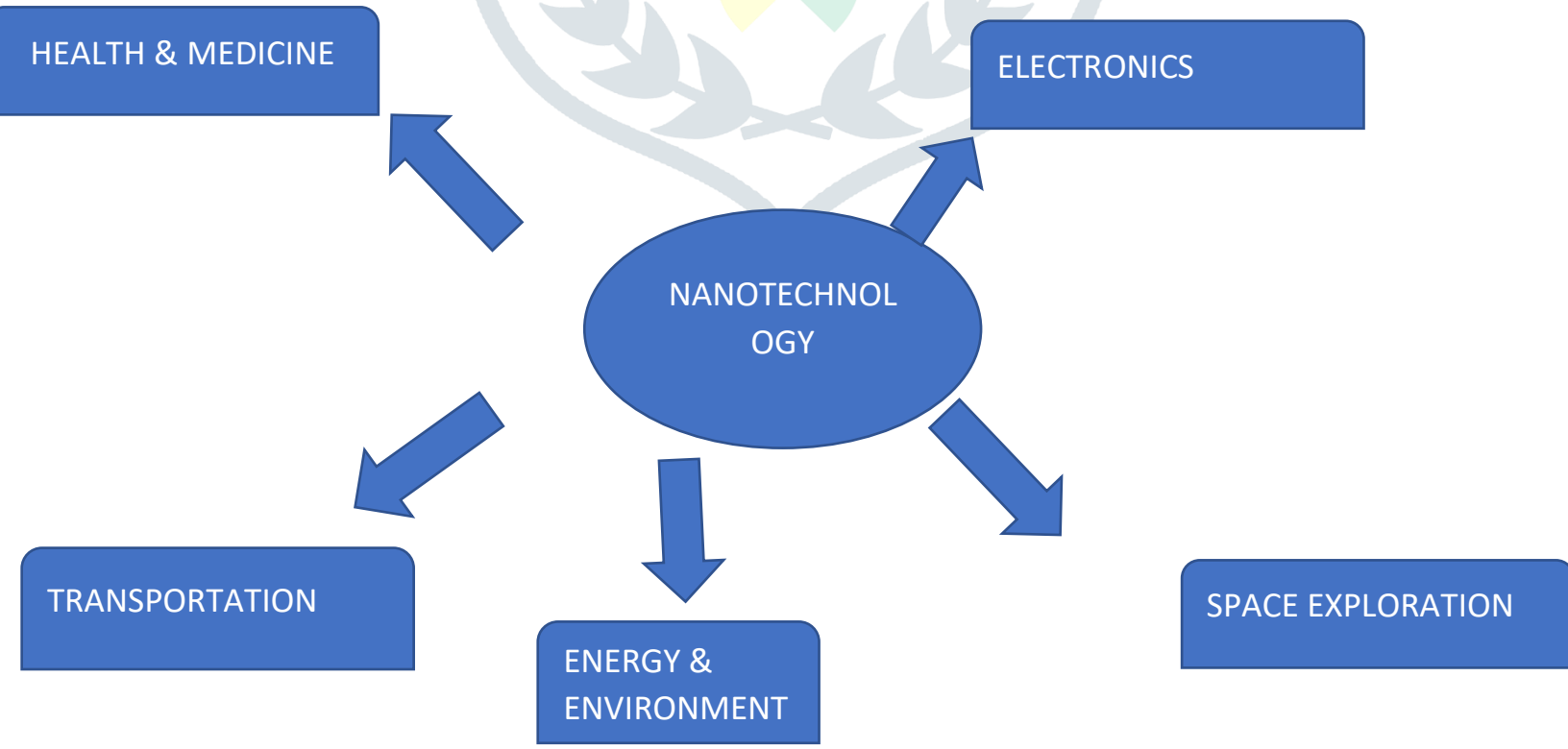
Nano- structure with particles size 1-100 nm. Produced using nanotechnology nowadays there is vast applications of nanotechnology is seen in several sectors specially in medicines for diagnosis of diseases

" The utilization of nanotechnology in human health benefits known as Nanomedicine , so nanotechnology has firmly entered the drug delivery to maximize drug therapeutics activity and minimize its undesirable side effects". [1]

By manipulating drugs and other materials at Nano- meter scale, the fundamental properties and bioactivity of the materials can be altered. These tools can be permitting a control over the different characteristics of drugs or agent [2].

Applications of nanotechnology

Nanotechnology has several applications in different fields as follows- nanotechnology now a days there is vast applications of nanotechnology is seen in several sectors specially in medicine for diagnosis of disease, drug delivery imaging and soon.



Introduction

From nanoparticles and bio-comparability it is used to improve the bioavailability of various drugs. Nano-fibres have surface area to volume ratio which increase its performance in several applications. Such as water filtration, tissue engineering scaffold, wounds, fibre composites, drug release and protective clothes [3].

In the nanotechnology nanomaterials are produced to target specific cells or tissue in the body . Nanomaterials are produced on a nanoscale level and it's safe to introduce in a body. Nanomedicine refers to the area of science that combines nanotechnology with drug to improve its ability to target specific cells. There are several applications of nanomaterials in the medicine gene delivers, detection of protein and pathogens probing of DNA structure, tissue engineering, tumour detection and separation of biological molecules and cells [2]. The molecular scale components like Nano- machinery are the long-term goal of Nanomedicine research. To better understanding of cellular mechanisms in having cells and to development of advanced technologies Nano-machinery in cells are useful. Molecular imaging has emerged as a powerful tool to visualize molecular events of an understanding disease, sometimes prior to its downstream manifestation.

Nanomaterials

According to the EC recommendation, nanomaterials refer to a natural, incidental or manufactured material comprising particles, either in unbound state or an aggregate. [4].

Applications of nanomaterials in Nanomedicine

For medicinal purposes of nanomaterials can be used to in three different areas-

1 Diagnosis (nondiagnostic)

2 Nano therapy (control drug delivery)

3 Regenerative medicines

Promising changes in clinical practice and the introduction of novel medicine for both diagnosis and treatment are holding by Nanomedicine.

- It is enabled to address unmet medical needs by an integrating effective molecule that otherwise could not be used because of their High toxicity".

  e.g., Mepact.

- Exploiting multiple mechanisms of action.
  e.g. Nanomag, multifunctional gels.
- Minimizing efficacy.
  e.g., By increasing bioavailability and reducing toxicity and dose.
- Providing drug targeting and favouring a preferential distribution with in the body.
  e.g., Improve transport across biological barriers. [5].

There are many advantages in the pharmaceutical development due to result of intrinsic properties of nanomaterials. Nanomaterials have specific surface area in relation to volume due to their small size.

Nanomaterials have a tendency to absorb the biomolecule. One of the most interaction with the living matter relies on the plasma or serum biomolecule absorption layer that forms on surface of colloidal nanoparticles, called as "corona". [6].

Applications of nanotechnology in medicine

Affecting at the molecular and atomic levels are the new areas of research for nanotechnology. To destroy the cancer cells nanomaterials shows very high efficiency nanomaterials might becomes an option to traditional cancer therapy because of nanomaterials can target specifically cancer cells and gives detailed imaging of tissue. Nano adjuvants with immunomodulatory properties used to deliver vaccine antigens and carbon nanotubes are a popular way of repairing damage tissue and might be used to regenerate nerves in the future [7]. Nanoparticles can be used in order to Nanomedicine pharmacokinetics, targeting efficiency and drug release profile [8].

Nanotechnology is the multidisciplinary field that is revolutionizing medicine. This technology has vast applications in treatment and prevention of HIV/AIDS for antiviral drugs in delivery active, targeting strategies have also been employed.

Major HIV reservoir cells contain macrophages have various receptor like formally peptide, mannose, FC receptor and galactose, which could be utilised for receptor mediator internalization. The drug stavudine was encapsulation using various liposomes (120-200) conjugated with galactose and mannose resulting in increase plain liposomes and generating significant level of the drug in liver, lungs and spleen. [9]. By protecting the delivered antigens from body fluids (e.g., lymph, serum and mucus) nanomaterials antigens encapsulation can increase the half life of an immunizing antigen. Nanomaterials can also be designed to effectively target APC's [10]. Convectional vaccine is mostly administration intramuscularly, but nanomaterials provide expanded opportunity for nasal and oral vaccination where mucosal immunity could be invaded. [11]. Treatment options for HIV may be improved using nanotechnology platform for drug delivery of antiviral drugs. In the future targeted codelivery of two or more antiviral drugs in nanoparticle system could radically improve treatment of viral reservoirs [12].

Nanotechnology- based drug delivery systems for the treatment of viral infections.

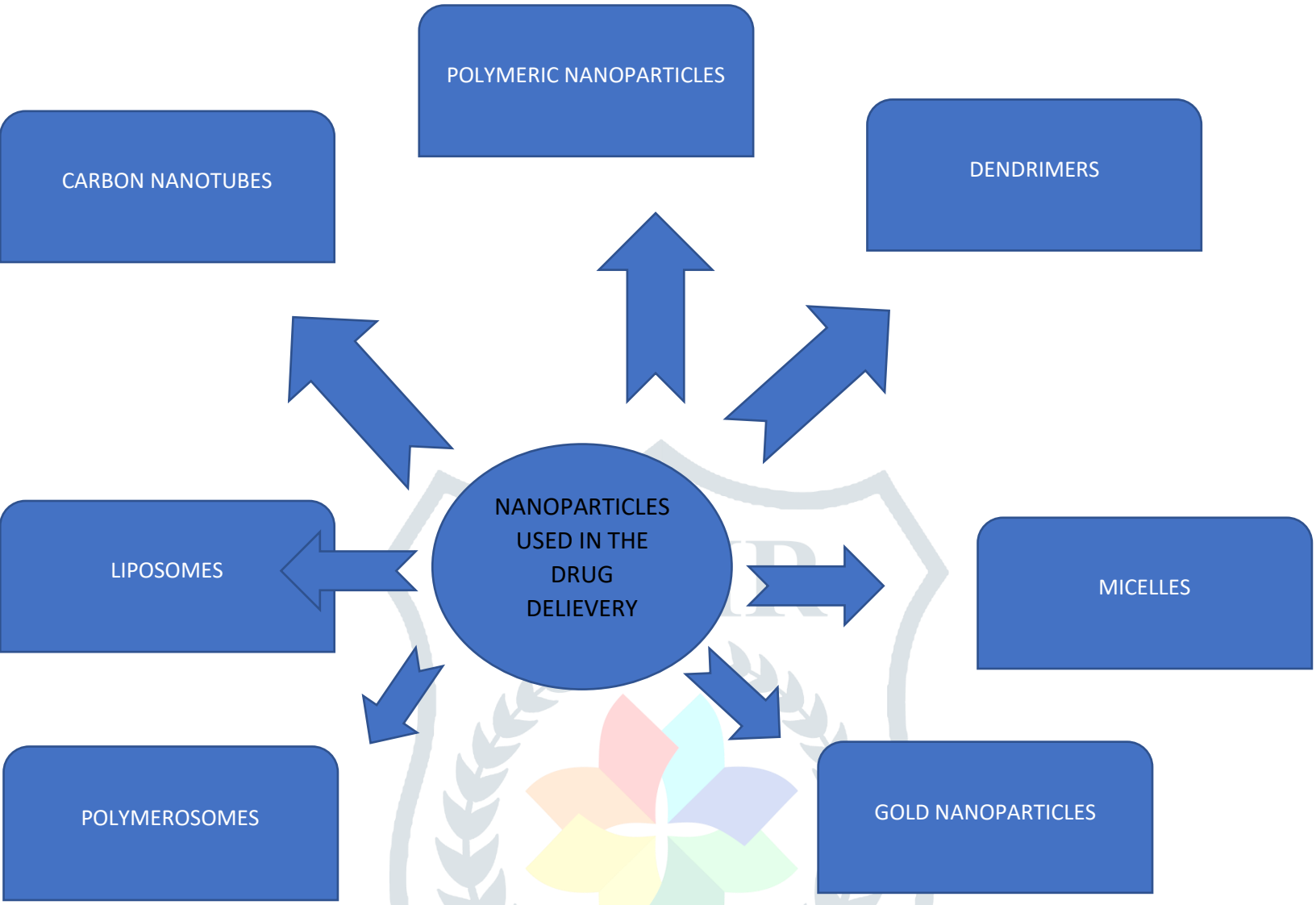
NANOPLATFORM	SIZE	DRUGS	VIRUS	RESULTS
1.INORGANIC NANOMATERIALS SELENIUM (Se)	100 nm	OTV	Influenza H1N1	High effectivity & cytotoxicity of Se@OTV in kidney cells infected with virus; higher viability of Se@OTV (93%) compared to free OTV (53%)
2.SILVER (Ag NPs)	2nm	AM	Influenza H1N1	Low cytotoxicity (90%) of Ag NPs loaded with AM
3.GOLD NPs	29.25nm	Interferon alpha	HCV	High stability of the Nano platform in human serum; sustained delivery of HA-AuNP/IFN Alpha for 7days.
4.PMA-coated MNPs	35.2nm	ENF	HIV	Increased drug translocation across the BBB; nontoxic in vivo & in vitro ENF-NPs.

5.ox-MWCNT	-	CHI360/CHI415	HIV	High antiviral activity; low cytotoxicity
6.Lipid-coated mesoporous silica nanoparticles (LCMSNs)	75nm	ML336 Antiviral immunostimulant	Venezuelan equine encephalitis virus (VEEV)	Decreased brain viral titer in infected mice compared to controls; absence of bioaccumulation in tissues; non-toxicity of LC-MSNs
7.PEG-PLGA	178-197nm	Diphyllin/bafilomycin	Influenza H1N1	Antiviral activity & biocompatibility; high safety of carrier; CC50 value of 12.5 & 21.89 micro-meter for free diphyllin & encapsulated diphyllin
8. PLGA	185nm	EFV	HIV	Increased bioavailability of NFV PLGA-NPs by 4.94-fold compared to free NFV
9.PLGA	116-143nm	GCV	HSV-1	Non-cytotoxic PLGA NPs after 24-48 h contact with HCEC Cells
10. Squalene-based NPs	-	Adenosine/Alpha-tocopherol	SARS-COV-2	High efficacy; potential to control inflammation

Reference [13]

Drug delivery:-

For specific drug delivery at site the nanoparticles are used in nanotechnology. Nanomedicine which are made up of nanoscale particles used for drug delivery which can improve drug bioavailability. For maximizing bioavailability both at specific places in the body and over a period of time, molecular targeting is done by Nano engineered device such as Nano robots .[14]. By regulated drug release tissue damage can be prevented with drug delivery. To leading the development of completely new drugs nanotechnology and nanoscience shows one of the major impact potential Nano drugs will by very specific and we'll understood mechanism having useful behaviour and less side effects. In early phase clinical trials for drug delivery minicell a nanoparticle is used for treatment of patients with untreatable and advanced cancer. In drug delivery Nano sponges are also important tools due to their porous nature and small size they can bind poorly soluble drugs with in their matrix and bioavailability will improve. They can be made to carry drugs to specific sites to this helps to prevent protein degradation and drug which can gives prolong drugs release in a controlled manner.



Nanotechnology in covid-19

The main role of nanotechnology i.e., Nanomedicine, which shows role in development of translatable therapeutics against different viral infection. Nanomedicine has already proven its activity against several infection disease including HBV[15], HIV, respiratory syncytial virus and influenza virus. In the field of nanotechnology many cov-relared parents have been reported.

Nanoparticles based vaccine against COV's

To rapidly control current and future COV outbreaks only vaccination is the best option. Nano vaccines are designed through different nanoparticles related mechanism like controlling regulations of prosing by APC's and antigen uptake, form nanoparticles matrix control the delivery of antigens.

Here is the table which summaries some developed Nano vaccines against pathogenic COV's. In this COV's is the prime candidate for Nano vaccines and 'S' protein is the main attachment factor. These are designed to improve vaccine efficiency and immunization strategies. These Nano vaccines are mainly developed via self-assembly or functionalization of gold nanoparticles [16].

Nanoparticles-based Vaccination against Coronavirus

Platform	Antigenic component	Virus	Notes
Spike protein NPs	Spike protein	SARS-CoV, MERS-CoV	Induce high level of neutralizing antibodies adjuvants improved safety & immunogenicity
Spike protein-displaying VLPs		MERS-CoV	Spike protein attaches DPP4 receptors, stimulating immune system
RBD- displaying VLPs	Gene of RBD of spike protein	MERS-CoV	Induced RBD-specific immune responses Antisera protected host cells from CoV infection
Chaperna based NPs		MERS-CoV	Induced mice immunization via interfering with binding of RBD to DPP4 Receptors
Polypeptide NPs	HRC1 epitope of spike protein	SARS-CoV	Specific, work against SARS-CoV & any enveloped virus
S-AuNPs	spike protein of avian CoV	Avian CoV	Significant improvement in vaccination potency
S-AuNPs	spike protein	SARS-CoV	Induced strong IgG responses lung eosinophilic immunopathology

Nanomedicine for combination drug therapeutics

For the treatment of covid-19 combination therapy is a one of the possibilities by giving lower dosage of the individual drug causing fewer side effects, achieving multiple and complimentary therapeutics target and reducing the likelihood of residence development several such combination for novel corona virus treated are documented in the WHO landscape information.

A variety of nanomaterials and combination and fabrication techniques enables the design of drug of drug combination with excellent control in preserving synergistic drug, overlapping pharmacokinetics and reducing combination allied side effects, loaded in Nano carriers. Like liposomes, dendrimers, core shell nanoparticles, polymeric and lipid polymeric Nano particles are described for co encapsulation of both hydrophilic and hydrophobic drugs.

“ Achieving the sequential release of two drugs, ratiomeric loading and controlled release of three drug, co delivery of RNA chemotherapeutic, and co delivery of Si RNA + micro-RNA “. [17]

“ A Nano suspension of LNP’s loaded with their ARV’s drug (two hydrophobic: lopinavir and ritonavir and one hydrophilic : tenofovir) has been formulated to overcome the lymph drug in efficiency of the oral combination of these drugs”. [18]

Combination Drug Treatments Proposed for COVID-19

Combination description	Candidates	Status
Protease inhibitors	Ritonavir + lopinavir	Under trial of covid-19
Non-nucleoside reverse transcriptase inhibitor + nucleotide reverse transcriptase inhibitor	Emtricitabine + tenofovir	Under trial of covid-19
Nucleoside inhibitor + protease inhibitor	Ribavirin + Ritonavir/lopinavir	Clinical study of SARS NCT00578825
Antiretroviral protease inhibitor + cobicistat	Darunavir + cobicistat	Under trial of covid-19
antiviral + type I interferons – signalling proteins made & released by host cells during viral infections	IFN + ribavirin	Clinical study of SARS
Interferons – signalling proteins made & released by host cells during viral infections + antiviral + steroid hormones	IFN + ribavirin + steroids	Clinical study of SARS, MERS
protease inhibitor + proteins made & released by host cells + antiviral	Ritonavir + lopinavir + IFN + ribavirin	Clinical study of MERS
Type I interferons - signalling proteins made & released by host cells during viral infections + immunosuppressant	IFN-beta1a + mycophenolate mofetil	Clinical study of MERS
Protease inhibitors + proteins made & released by host cells	Ritonavir + lopinavir + IFN-beta1b	Clinical study of MERS
Synthetically developed recombinant type I interferon + steroid hormones	IFN alfacon-1 + corticosteroids	Clinical study of MERS

Conclusion

The advantages of nanotechnology can be seen across medicine, genomics and vaccines. Interactions of biomolecules & cells due to their peculiar size, shape, chemical composition, surface structure, charge can be greatly influence by the properties of nanomaterials. Nanotechnology tools also play a pivotal role in advancing COVID-19 treatment & vaccine development. A m-RNA based vaccine employing nanoparticle (LNPs) delivery is already in clinical trials. By further research in nanotechnology, it can be useful for every aspect of human life.

Reference

1. Shi J, Votruba AR, Farokhzad OC, Langer R. Nanotechnology in drug delivery and tissue engineering: from discovery to applications. Nano Lett. 2010 Sep 8;10(9):3223-30. doi: 10.1021/nl102184c. PMID: 20726522; PMCID: PMC2935937.

2. Rajiv Saini, Santosh Saini and Sugandha sharma nanotechnology : the future medicine doi 10.4103/0974-2077.63301

3. Ghajarieh A, Habibi S, Talebian A. Biomedical Applications of Nanofibers. Russ J Appl Chem. 2021;94(7):847–72. doi: 10.1134/S1070427221070016. Epub 2021 Oct 5. PMCID: PMC8491758.

4. Ghajarieh A, Habibi S, Talebian A. Biomedical Applications of Nanofibers. Russ J Appl Chem. 2021;94(7):847–72. doi: 10.1134/S1070427221070016. Epub 2021 Oct 5. PMCID: PMC8491758.

5. Yang R, Wei T, Goldberg H, Wang W, Cullion K, Kohane DS. Getting Drugs Across Biological Barriers. Adv Mater. 2017 Oct;29(37):10.1002/adma.201606596. doi: 10.1002/adma.201606596. Epub 2017 Jul 28. PMID: 28752600; PMCID: PMC5683089.

6. Auría-Soro C, Nesma T, Juanes-Velasco P, Landeira-Viñuela A, Fidalgo-Gomez H, Acebes-Fernandez V, Gongora R, Almendral Parra MJ, Manzano-Roman R, Fuentes M. Interactions of Nanoparticles and Biosystems: Microenvironment of Nanoparticles and Biomolecules in Nanomedicine. Nanomaterials (Basel). 2019 Sep 24;9(10):1365. doi: 10.3390/nano9101365. PMID: 31554176; PMCID: PMC6835394.

7. Zhu M, Wang R, Nie G. Applications of nanomaterials as vaccine adjuvants. Hum Vaccin Immunother. 2014;10(9):2761-74. doi: 10.4161/hv.29589. Epub 2014 Nov 17. PMID: 25483497; PMCID: PMC4977448.

8. Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology. Saudi Pharm J. 2018 Jan;26(1):64-70. doi: 10.1016/j.jsps.2017.10.012. Epub 2017 Oct 25. PMID: 29379334; PMCID: PMC5783816.

9. Mamo T, Moseman EA, Kolishetti N, Salvador-Morales C, Shi J, Kuritzkes DR, Langer R, von Andrian U, Farokhzad OC. Emerging nanotechnology approaches for HIV/AIDS treatment and prevention. Nanomedicine (Lond). 2010 Feb;5(2):269-85. doi: 10.2217/nnm.10.1. PMID: 20148638; PMCID: PMC2861897.

10. Zhu M, Wang R, Nie G. Applications of nanomaterials as vaccine adjuvants. Hum Vaccin Immunother. 2014;10(9):2761-74. doi: 10.4161/hv.29589. Epub 2014 Nov 17. PMID: 25483497; PMCID: PMC4977448.

11. Yusuf H, Kett V. Current prospects and future challenges for nasal vaccine delivery. Hum Vaccin Immunother. 2017 Jan 2;13(1):34-45. doi: 10.1080/21645515.2016.1239668. Epub 2016 Dec 9. PMID: 27936348; PMCID: PMC5287317.

12. Mamo T, Moseman EA, Kolishetti N, Salvador-Morales C, Shi J, Kuritzkes DR, Langer R, von Andrian U, Farokhzad OC. Emerging nanotechnology approaches for HIV/AIDS treatment and prevention. Nanomedicine (Lond). 2010 Feb;5(2):269-85. doi: 10.2217/nnm.10.1. PMID: 20148638; PMCID: PMC2861897.

13. Hasanzadeh A, Alamdaran M, Ahmadi S, Nourizadeh H, Bagherzadeh MA, Mofazzal Jahromi MA, Simon P, Karimi M, Hamblin MR. Nanotechnology against COVID-19: Immunization, diagnostic and therapeutic studies. J Control Release. 2021 Aug 10;336:354-374. doi: 10.1016/j.jconrel.2021.06.036. Epub 2021 Jun 25. PMID: 34175366; PMCID: PMC8226031.

14. Enhanced oral bioavailability through nanotechnology in Saudi Arabia: A meta-analysis Nawzat D.Al Jbour 19 October 2021, Accepted 17 January 2022, Available online 21 January 2022, Version of Record 1 February 2022.

15. Singh L, Kruger HG, Maguire GEM, Govender T, Parboosing R. The role of nanotechnology in the treatment of viral infections. Ther Adv Infect Dis. 2017 Jul;4(4):105-131. doi: 10.1177/2049936117713593. Epub 2017 Jul 5. PMID: 28748089; PMCID: PMC5507392.
2017 May 22. doi: 10.3390/molecules22050857

16. Applications of Gold Nanoparticles in Nanomedicine: Recent Advances in Vaccines † Sónia Alexandra Correia Carabineiro Margaret A. Brimble CNZM

17. Chen X, Mangala LS, Rodriguez-Aguayo C, Kong X, Lopez-Berestein G, Sood AK. RNA interference-based therapy and its delivery systems. Cancer Metastasis Rev. 2018 Mar;37(1):107-124. doi: 10.1007/s10555-017-9717-6. PMID: 29243000; PMCID: PMC5898634.

18. Gao Y, Kraft JC, Yu D, Ho RJY. Recent developments of nanotherapeutics for targeted and long-acting, combination HIV chemotherapy. Eur J Pharm Biopharm. 2019 May;138:75-91. doi: 10.1016/j.ejpb.2018.04.014. Epub 2018 Apr 17. PMID: 29678735; PMCID: PMC6482852.