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Precision medicine: An Advanced Approach Towards Novel Drug Delivery System

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ABSTRACT: -Precision medicine is an advanced approach towards novel drug delivery system, because in our India the treatment is based on trial-and-error method and they don't consider the idiosyncrasy of the patient, but in precision medicine, the physician considers the patient factors like environmental conditions, genetic factors, life style and food habits. In general treatment, they follow one size fits all approach, but in precision medicine they follow patient idiosyncrasy factor. In general treatment, the diagnosis, prevention and prognosis of the disease is primitive, but in precision medicine it is more advanced approach and it is also known as revolutionary approach, where advanced technology, genetic science, artificial intelligent and novel drug delivery approach is used for treatment, diagnosis and prognosis of a disease. In this research, precision medicine in Parkinson's disease, extracellular vesicles and nanoparticles which are novel drug delivery carriers involved in Precision medicine are discussed in detail.

I. INTRODUCTION: -

Pharmaceutics is the discipline of pharmacy that deals with the process of turning a new chemical entity or old drugs into a medication to be used safely and effectively by patients. It is also called the science of dosage form design. There are many chemicals with pharmacological properties, but need special measures to help them achieve therapeutically relevant amounts at their site of actions. Pharmaceutics helps relate the formulation of drugs to their delivery and disposition in the body.

Conventional drug delivery system: - Drug delivery is a broad field of research on the development of novel materials or carrier systems for effective therapeutic delivery of drugs. The drug delivery may be steady, controlled, or targeted drug delivery and is commonly used methods. Since the advent of medical application systems, numerous drugs are being administered through various conventional drug delivery dosage forms such as solutions, lotions, mixtures, creams, pastes, ointments, powders, suppositories, suspensions, injectables, pills, immediate release capsules and tablets, etc., and so on to treat various diseases**.**
These conventional drugs have its own disadvantages, to minimize the demerits, novel drug delivery system came to light.

NOVEL DRUG DEIVERY SYSTEM: -Non-conventional, non-traditional means newer or novel, it is another methodology or a new approach for drug delivery other than the conventional drug delivery system. A novel drug delivery system can be defined as a new approach that combines innovative development, formulations, new technologies, novel methodologies for delivering pharmaceutical compounds in the body as needed to safely achieve its desired pharmacological effects. It may include scientific site targeting within the body, improve drug potency, control drug release with prolonged pharmacological effect. It involves the development of novel, better and safer drugs with long half-life and large therapeutic indices.
The treatment that followed in our India is mostly trial and error method because most of the diseases are idiopathic in nature, and there is no precise treatment for a particular patient and mostly none of the treatment consider the idiosyncrasy factor. The above-mentioned drug delivery systems having its own disadvantages and there is a need of precise treatment of particular patient for future support.

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In this realization, precision medicine revolutionary concept is being trigged to treat the patients with more advancement of technology and medicine in biotechnology, genetics, data science, artificial intelligence and pharmaceutical industry.

PRECISION MEDICINE: - According to precision medicine initiative, precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person". This approach will allow doctors and researchers to predict more accurately which treatment and prevention strategies for a particular disease will work in which groups of people. It is in contrast to a one-size-fits-all approach, in which disease treatment and prevention strategies are developed for the average person, with less consideration for the differences between individuals.

According to "National institute of health, precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person".

AIM AND OBJECTIVE: - The main aim of precision medicine is "to deliver the right dose, to the right person, at right time. These are the following objectives that precision medicine focus on

- Shift the emphasis in medicine from reaction to prevention
- Predict susceptibility to disease
- Improve disease detection
- Preempt disease progression
- Customize disease-prevention strategies
- Prescribe more effective drugs avoid prescribing drugs with predictable side effects
- Reduce the time, cost, and failure rate of pharmaceutical clinical trials
- Eliminate trial and error inefficiencies that inflate health care costs and undermine patient care.

Precision medicine mostly consider the following terms to treat the patient effectively

- Genomics
- Metabolomics
- Proteomics
- Microbiome
- Pharmacogenomics
- Nutraceuticals

Personalized medicine is a multi-faced approach to patient care that only improves our ability to diagnose and treat disease but offers the potential to detect disease at an earlier stage, when it is easier to treat effectively. The full implementation of personalized medicine encompasses:

a) **Risk assessment**: Genetic testing to reveal predisposition to disease
b) **Prevention**: Behaviour / Lifestyle/ Treatment intervention to prevent disease
c) **Detection**: Early detection of disease at the molecular level
d) **Diagnosis**: Accurate disease diagnosis enabling individualized treatment strategy
e) **Treatment**: Improved outcomes through targeted treatments and reduced side effects
f) **Management**: Active monitoring of treatment response and disease progression.

II. PRECISION MEDICINE IN PARKINSONS DISEASE: -

Parkinson's disease is primarily associated with the gradual loss of cells in the substantia nigra of the brain. This area is responsible for the production of dopamine. Dopamine is a chemical messenger that transmits signals between two regions of the brain to coordinate activity. For example, it connects the substantia nigra and the corpus striatum to regulate muscle activity. If there is deficiency of dopamine in the striatum the nerve cells in this region "fire" out of control. This leaves the individual unable to direct or control movements. This leads to the initial symptoms of Parkinson's disease. As the disease progresses, other areas of the brain and nervous system degenerate as well causing a more profound movement disorder. The exact cause for the loss of cells is unknown. Possible causes include both genetic andenvironmental factors.

According to Christian U. von Lin stow, ZivGan- and PatrikBrundin, published in translational Neurodegenerative,there are some limitations of the selected disease targets such as the considerable heterogenicity with Parkinson's disease patients. The annual economic expenditure associated with 6,30,000 Parkinson's disease patients in the US in 2010 were estimated to be around $14.4 billion and this expense is rapidly increasing given an anticipated prevalence to reach 12,38,000 cases in 2030. Therefore, developing disease modifying treatments is of the utmost important at present. Symptomatic treatment of PD with, e.g., drugs targeting the dopamine system, has become increasingly "personalized" with multiple drugs and delivery systems being used according to the specific individual needs of each

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patient.However, when trying to achieve disease modification, a "precise" approach based on the molecular underpinnings of the disease in each patient, has not yet been fully tested. In 1–2% of PD cases, the cause of PD is attributed to the highly penetrant, autosomal dominant and recessive genes; in 5–10% of PD cases, PD is associated with strong risk genes (e.g., LRRK2 and GBA mutations); and the remaining cases are idiopathic without a single identifiable cause.

PD patients with LRRK2 mutations: - LRRK2 is a large multifunctional and multidomain protein expressed particularly by immune cells (e.g., microglia and macrophages) and in tissues including kidney, lung and, to a much lower extent, brain. It plays important roles in inflammation, DA receptor trafficking, synaptic vesicle endocytosis and protein degradation among others. Several variants in the LRRK2 gene have been associated with increased or decreased risk of PD, the autoimmune disorder Crohn's disease, and the exacerbated immune response in leprosy. The most common G2019S variant accounts for up to 1% of sporadic and 4% of familial PD and among Ashkenazi Jews as much as 10 and 28% respectively and in North African Arabs 36 and 39% respectively. Other PD-associated LRRK2 variants include R1441G/C/H, Y1699C/G, R1628P, G2385R and I2020T. Some of these variants show varied penetrance depending on the ethnicity and where the individuals live, underlining that the genetic and environmental disease-modifiers remain to be identified. Current reports of the pathophysiological mechanism behind LRRK2-PD suggest a toxic gain-of function mechanism generated from the increased kinase activity caused by variants in the MAPKKK domain (G2019S, I2020T) or indirectly by variants in the COR domain (Y1699C/G) or ROC domain (R1441G/C/H) that reduce the GTPase activity. The LRRK2 levels in the CSF are more increased in PD patients with the G2019S risk variant. The rationale behind current drug trials aiming for LRRK2 inhibition in PD is principally based on this idea and also on a study reporting increased wild-type LRRK2 kinase activity in idiopathic PD.It has been suggested that it is desirable to reduce elevated LRRK2 in neurons in PD, but the levels of LRRK2 expression are higher in immune cells in the brain and in peripheral organs. This may indicate multiple prime disease mechanisms, of which one may be more important than others. Furthermore, the multiple roles of LRRK2 and our limited understanding of the contribution of each protein domain in relation to this, may also be a simplification.

Drug trials targeting LRRK2 hyperactivity in PD: - Denali Therapeutics, has recently finished a double blinded, placebo-controlled phase IB [elderly adults aged 80 years and over] drug trial on a small molecule, LRRK2 inhibitor DNL201, and reported a > 50% inhibition of phosphorylated (p) LRRK2 (pS935) in blood, which is a direct measure of activity, and pRAB10, which is a downstream target of LRRK2 in peripheral blood mononuclear cells in idiopathic PD patients. The researchers also observed a 20–60% reduction in lysosomal biomarker bis-monoacylglycerol phosphate (BMP) in urine (ClinicalTrials.gov ID: NCT03710707). This has been followed by a similar trial of the small molecule LRRK2 inhibitor DNL151 currently in phase IB, which has shown a generally safe adverse-effect profile but also a substantial inhibitory effect on pS935 LRRK2 and pRAB10 alongside reductions in urine BMP.This study is expected to complete in Mid-2020 (ClinicalTrials.gov ID: NCT04056689). Denali Therapeutics, intends to select either DNL201 or DNL151 to advance into phase 2. Ionis Pharmaceuticals, is currently testing the LRRK2 antisense oligonucleotide drug BIIB094 administered intrathecally in a placebo-controlled phase I drug trial to evaluate the safety profile (ClinicalTrials.gov ID: NCT03976349).These drug trials are investigating the effects of LRRK2 inhibition in PD patients with or without LRRK2 risk variants though challenged by the relatively low frequency of risk variant-carriers and the even more challenging effort of recruiting patients with identical risk variants. Finally, it is interesting to note that none of the drug trials to our knowledge have considered employing non-risk-variant carriers with base levels of LRRK2 as an important inclusion criterium though this would further refine the strategy of precision.

PD patients with GBA mutations: - The GBA gene codes for the enzyme glucocerebrosidase (GCase) that facilitates the lysosomal breakdown of sphingolipids (e.g., glucosylceramide into glucose and ceramide), and is expressed in most cells, notably in the macrophage lineage. The characteristic swollen macrophages (i.e., Gaucher cells) contain accumulation of intracellular glucosylceramide and infiltrate organs, causing organomegaly in Gaucher disease. Further evidence has suggested extensive involvement of the adaptive immune system including B- and T-cell recruitment and maturation, respectively. More

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than 300 GBA variants have been associated with Gaucher disease with varied degrees of nervous system involvement, while 130 GBA variants have been estimated to be linked with the PD risk, diversely affecting the disease risk, onset and progression depending on the mutation severity.Some variants can also affect the risk of Lewy body dementia. Depending on the population, about 5–20% of idiopathic PD cases are associated with GBA variants.Among Ashkenazi Jews, as many as 18–20% of PD patient have GBA variants associated with the elevated PD risk. The PD-associated variants in the GBA gene have been proposed to be associated with reduced GCase activity.Different GBA risk variants may decrease the GCase activity by different ways, including directly causing a loss of enzyme activity, failing to comply with endoplasmic reticulum (ER) quality control causing proteasomal degradation, perturbating trafficking to the lysosome due to ER or Golgi retention or the inability to properly connect with the lysosomal transporter LIMP2 or lysosomal activator protein Saposin C.The rationale behind the clinical trials in PD targeting GBA risk variants is to correct cellular GCase deficiency. It may however also be relevant for some idiopathic PD patients since reduced GCase activity has been found in several brain regions and in the CSF of these patients. Current approaches to correct these impairments include the use of pharmaceutical chaperones, gene therapy, enzyme activators and substrate reduction therapies. Pharmaceutical treatment of Gaucher disease with enzyme replacement therapy or GCase enhancers has proven effective, however, when repurposing these drugs for PD treatment, a major challenge comes with respect to their poor ability to cross the blood-brain barrier (BBB).This means that these drugs would be used in very high dosages compared to the treatment of Gaucher disease to ensure that sufficient drugs cross the BBB, which will raise an important objective of profiling adverse effect.

Drug trials targeting GBA impairments in PD: - The pharmaceutical company PRO.MED.CSA recently finished a phase II non-randomized and non-controlled clinical trial of the FDA-approved mucolytic and CGase chaperone Ambroxol (ClinicalTrials.gov ID: NCT02941822).They reported that the orally administered Ambroxol was detectable in blood and CSF in PD patients without any serious adverse effects after 186 days and that this was paralleled by a small reduction in GCase activity in the CSF caused by the inhibitory effects of Ambroxol at neutral pH.They also detected an increase in CSF α-syn and reduced tau in serum by ELISA, which were paralleled by improvement in the total MDS-UPDRS score (62.6 ± 32.2 versus 53.9 ± 30.3) and worsening in the NMSS score (49.3 ± 36.1 versus 60.8 ± 38.6). However, the interpretation of these tests was difficult because of the lack of a placebo group. Another Ambroxol drug trial designed to be double-blinded and placebo-controlled has been initiated by Weston Brain Institute, University of Western Ontario and London Health Sciences Centre and is currently in phase II, expecting a late-2020 completion (ClinicalTrials.gov ID: NCT02914366). Other current clinical trials targeting GBA include Sanofi's glucosylceramide synthase inhibitor GZ/SAR402671 in a phase II double-blinded and placebo-controlled trial finishing in early 2023 (ClinicalTrials.gov ID: NCT02906020) and resTORbio's TORC1 inhibitor RTB101 phase IB/IIA trial. RTB101 is also under test in combination with rapamycin (Sirolimus) and will finish in late 2020 (ANZCTR ID: ACTR N12619000372189); interim results showed that the drugs are well tolerated and can cross the BBB.Prevail Therapeutics' intracisternally administered GBA-coding AAV9 viral vector PR001A, is currently in a phase I/II double-blinded and sham-procedure controlled trial, which is expected to complete in 2026 (Clinical Trials. - gov ID: NCT04127578).Lysosomal Therapeutics is testing a small molecule GCase activator LTI-291 in a phase IB safety trial (Trialregister.nl ID: NTR7299). The finished Ambroxol trial tested PD patients with or without GBA risk variants similar to the ongoing trials studying the effects of GZ/SAR402671 and RTB101, while the PR001A and LTI-291 drug trials are exclusively recruiting PD patients with GBA risk variants. In the ongoing Ambroxol trial, recruited PD patients are screened for the presence of GBA risk variants. Recruiting PD patients with GBA risk variants presents the same difficulties as recruiting PD patients with LRRK2 risk variants, including low frequency of risk variant carriers and difficulty in collecting patients with identical risk variants. Further considering GCase levels as an inclusion criterium in non-GBA risk variant carriers would be relevant to refine the strategy of precision.

III. EXTRACELLULAR VESICLES IN PRECISION MEDICINE: -

According to Jonathan M. Carnino, ZhiHao Kwok and Yang Jin published in frontiers in medicine,Extracellular vesicles (EVs) are cell-

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derived, membrane-bound nanoparticles which are secreted by nearly all cell types and play a known role in cell-to-cell crosstalk. EVs contain and transport a variety of "cargo" including lipids, proteins, and nucleic acids. Based on their physical sizes, biogenesis, and surface markers, EVs were previously classified into three main categories, namely the apoptotic bodies (ABs), micro vesicles (MVs) and exosomes. ABs are regarded as secreted vesicles by cells undergoing apoptosis and typically range 1,000–5,000 nm in size. micro vesicles, on the other hand, are generated by the outward budding and consequent pinching of the plasma membrane and measure 100–1,000 nm in size. Lastly, exosomes are formed from the maturation of intraluminal vesicles as multivesicular bodies before their fusion with the plasma membrane for secretion. The size of exosomes typically ranges between 30 and 100 nm. Recently, the lack of consensus on specific surface markers for these three categories, coupled with the overlap in their physical sizes, prompted the discontinuation of the aforementioned nomenclature for EV classification. Instead, guidelines set by the International Society of Extracellular Vesicles suggest that EVs can be termed based on:

a) Physical characteristics of EVs, such as size ["small EVs" and "medium/large EVs," with ranges defined, for instance, respectively, 200 nm (large and/or medium)] or density (low, middle, high, with each range defined);
b) Biochemical composition (CD63+/CD81+-EVs, Annexin A5-stained EVs, etc.); or
c) Descriptions of conditions or cell of origin (podocyte EVs, hypoxic EVs, large oncosomes, apoptotic bodies)".

Evs in respiratory diseases: current diagnostic and therapeutic applications of EVS: - Asthma is a chronic respiratory illness characterized by airway narrowing in response to a variety of stimuli. One study which analysed the cargo miRNA profile of exosomes in patients with asthma found significant alterations in BALF [bronchoalveolar lavage fluid] exosomal miRNA for 24 miRNAs, including the let-7 and miR-200 families. Notably, BALF collection from patients is an overly invasive method to diagnose asthma, however this study proved EVmiRNA profiling can be used diagnostically in the disease. Another report analysed exosomes in nasal lavage from patients with asthma and chronic rhinosinusitis. They found nasal lavage exosomes to induce the migration of innate immune cells, and that these exosomes carried a reduced number of barrier and antimicrobial proteins compared to healthy patients. Another report, which was notably the first group to detect miRNAs from exhaled breath condensate, hypothesized that the ability to detect them can be contributed to the stability offered from their encapsulation within exosomes. Testing in patients with asthma and tuberculosis, compared to healthy individuals, they found that miRNA profiles isolated from exhaled breath condensate reflected general inflammatory processes and/or epithelial damage. These findings show EVs collected from a much less invasive procedure such as nasal lavage, or even from exhaled breath, can be analysed and have clinical implications for disease progressions.

Chronic obstructive pulmonary disease (COPD) is the cumulative name for a number of diseases that share the common element of limited expiratory airflow. The American Thoracic Society defines COPD as chronic bronchitis and emphysema. The role of EVs in COPD has been of interest lately and many reports have focused on understanding the significance of EVs in the disease processes. Numerous EV-miRNAs have been reported to be upregulated in the BALF, serum, and plasma of COPD patients. Specifically, analysis of exosomal-miRNA from BALF shows an upregulation of miR-223-3p, −223-5p, −338-3p, −1469, −204-5p, and−618. Analysis of exosomal-miRNA from serum shows an increased expression of miR-21 and MV-miRNA from plasma shows an increased expression of miR-191, −126, and−125a. These reports build on the case that EV-miRNA from biological fluids can serve as a useful tool in diagnosing patients with COPD.

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive type of interstitial lung disease characterized by fibrosis and deteriorating lung function. Compared to asthma and COPD, there has been much less research into EV-miRNA diagnostic markers for IPF. One recent report found serum EV-miR-21-5p to be elevated in patients with IPF compared to control. Although these findings suggest serum-EV-miR-21-5p may be a suitable diagnostic marker for IPF, further studies are necessary to uncover additional EVmiRNAs expressions altered in the setting of IPF.

Acute lung injury (ALI) is a devastating illness characterized by non-cardiogenic pulmonary edema, vascular leakage, inflammation, and lung epithelial injury. Extensive research been done to reveal miRNAs involved in ALI and inflammation, however very few groups have studied EV-

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miRNAs in these settings. Recently, increased expression of BALF MV-miR-185- 5p was reported to induce necroptosis and apoptosis in type II lung epithelial cells. Another recent study suggests increased expression of MV-miR-223/142 plays a role in the pathogenesis of lung macrophage-mediated lung responses and this upregulation could be detected in both BALF and serum. Furthermore, MV-miR-17/221 and MV-miR-320a has been shown to induce macrophage recruitment and subsequently contribute to lung inflammation. Additionally, increased expression of the EV-miR-466 family has been shown to exacerbate inflammation via the NLRP3 inflammasome pathway. Of note, all of these mentioned reports were in mouse models and there is a significant lack of clinical research into EV-miRNAs in ALI and inflammation. Due to the limited studies into EV-miRNAs involved in ALI and inflammation, further work is necessary to completely uncover the role EV-miRNAs play in this disease and develop a diagnostic panel that could be used clinically.

Lung cancer is the primary cause of cancer-related deaths in the world and accounts for about 25% of all cancer mortality. In one clinical study including 21 patients with lung cancer and 25 control patients, EV-miRNAs isolated from pleural lavage showed an upregulation of EV-miR-150-5p, −27a-5p, −21-3p, −1249-3p, and−485-5p and a downregulation of EV-miR-144 -5p, −1-3p, −584-5p, −133b, −451a, −199a-5p, −20b-5p, −181c-5p, and−30e-5p in cancer patients. This study showed that in the clinical setting, EV-miRNAs isolated from pleural fluids are a potential source of biomarkers for lung cancer. These results have promise for being used to develop a potential diagnostic panel for lung cancer. An additional study which analysed EV-miRNAs from plasma in patients with lung cancer, found an increased expression of EV-miR-21, −191, and−192 in patients with lung cancer. A useful and interesting addition to these studies would've been to see how the level of expression correlated with prognosis, which would allow an EV-miRNA panel to be used by physicians in providing patients with an accurate prognosis.

Malignant Pleural Mesothelioma (MPM) is a form of cancer manifesting in the pleural cavity, and its incidence is strongly correlated with a past asbestos exposure. The relationship between asbestos exposure and MPM is well-documented and has a latency time between 30 and 40+ years. One recent clinical study, which included 23 MPM patients and 19 cancer free subjects with a history of asbestos exposure, suggested that EV-miR-103a-3p and miR-30e-3p isolated from plasma was upregulated in MPM patients compared to the control subject. This study has been the only one carried out to analyse EV-miRNA profiles in patients with MPM. Additional pleural diseases such as pleurisy, pleural effusion, pneumothorax, and hemothorax lack any research into EV-miRNAs related to these illnesses.

IV. NANOPARTICLES IN PRECISION MEDICINE: -

According to Jianhua Yang, ChengyouJia, Jianshe Yang, published in Ivy spring International Publisher, From a scientific perspective we know the engineering nanomaterials have significant priority to promoting disease diagnosis and treatment. Nanotechnology can facilitate the drug delivery through nanomaterials targeted modification, transport of desired molecules to specific organelles. The nanotechnology program has thrived worldwide in the past 20 years ago, such as the US National Science and Technology Council (NSTC) launched the National Nanotechnology Initiative (NNI) in 2000, and presented clear plans and major challenges in this field. Nanoparticles (NPs) occupy a large part of all the plans with the source variation and preparation diversity. The improvement in stability and solubility of the NPs depends on many factors including the NP composition, formulation, chemical structures of the small drug molecules and its carriers, temperature, pH, etc., thus improving the safety and effectiveness. Owning these priorities, NPs have been widely used and produced promising results both in pre-clinical and clinical stages. As nanoparticle-based precision therapies are applied in a broad area, such as cancer therapy, immunotherapy, and recently in virus infected disease, a full span and timely understanding of NPs progress is particularly important. Here we will report and review several most commonly used NPs in the terms of its preparation and precision medicine application, and expect to afford the guidance to optimize the strategies from its design to clinical application.

Applications of nanomaterials in precision medicine have emerged since the launch of the Precision Medicine Initiative (PMI) in 2015. An early clinical detection for personalized biomolecular adsorbed on graphene oxide nanosheets was exerted with pancreatic cancer patient blood in 2019. Graphene oxide can combine

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the unique characteristics of a small amount of albumin to enable strong adsorption of low-level proteins present in plasma. Other magnetic NPs or AuNPs showed the priority in biomarker detection analysis with much less time and consumes. Beside the diagnostic usage, some of NPs can reshape the tumour microenvironment, thereby enhancing the sensitivity of tumours to specific treatments. Endothelial cells of tumours can be manipulated by the microRNA delivered by NPs, therefore alters the vascular system microenvironment and makes the tumour much more sensitive to conventional cancer therapies. Similar bioinspired lipoproteins have been used to reshape tumours and increase NPs accessibility to cancer cells by 27 times. The use of photothermal NPs can improve the wettability and anti-solid tumour activity of CAR-T cells or lead the direct physical destroy to tumours or viruses. NPs can also regulate immune function and make cancer cells sensitive to treatment, homogenize environments, and make more patients respond to accurate treatment.

CONCLUSION: -

In India ayurveda is the only medical practice for the treatment of various types of diseases but after British invasion, allopathy came to light and it evolved into many forms with the help of advanced technology. Now it is evolved as precision medicine where patient care is based on idiosyncrasy factor and moreover, thanks to human genomic project which lend a hand for revelatory aspect of this precision medicine, in this era, the diagnosis and treatment of disease is based on the screening of genes or DNA in an individual and then find out the root cause of the diseases.

In this above research, the authors intention is to highlight the concept of precision medicine and how this accroach is advanced towards the novel drug delivery system. But in fact, this research is only relay on the different sources and knowledge of the author which combines and present in this research.

The authors suggest you, that this concept is not complete and can procced in detailed study, in the future. Because, the research is only focus on proving how this is advanced towards novel drug delivery, but this concept is not reached its peaks yet, because it is still in progress, and there is lot of conclusions which opposes the concept that we presented in challenging facing section. Even in India, the precision medicine initiative was started in 2020 and the government funded with lot of money which is nearly 238 crore rupees. This project was known as genome Indian project funded by Indian department of biotechnology with the collaboration between 20 Indian research institutes, where Indian institute of sciences centre for brain research will be serving as its nodal point.

REFERENCES

[1]. Nalls MA, Blauwendraat C, Vallerga CL, Heilbron K, Bandres-Ciga S, Chang D, et al. Identification of novel risk loci, causal insights, and heritable risk for Parkinson's disease: a meta-analysis of genome-wide association studies. Lancet Neurol. 2019;18(12):1091–102.

[2]. Ball N, Teo WP, Chandra S, Chapman J. Parkinson's disease and the environment. Front Neurol. 2019; 10:218.

[3]. Barone P, Antonini A, Colosimo C, Marconi R, Morgante L, Avarello TP, et al. The PRIAMO study: a multicentre assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. MovDisord. 2009; 24(11):1641–9.

[4]. Blauwendraat C, Nalls MA, Singleton AB. The genetic architecture of Parkinson's disease. Lancet Neurol. 2020;19(2):170–8.

[5]. Cheng HC, Ulane CM, Burke RE. Clinical progression in Parkinson disease and the neurobiology of axons. Ann Neurol. 2010;67(6):715–25

[6]. Johnson ME, Stecher B, Labrie V, Brundin L, Brundin P. Triggers, facilitators, and aggravators: redefining Parkinson's disease pathogenesis. Trends Neurosci. 2019;42(1):4–13.

[7]. Kowal SL, Dall TM, Chakrabarti R, Storm MV, Jain A. The current and projected economic burden of Parkinson's disease in the United States. MovDisord. 2013;28(3):311–8.

[8]. Leonard H, Blauwendraat C, Krohn L, Faghri F, Iwaki H, Ferguson G, DayWilliams AG, Stone DJ, Singleton AB, Nalls MA, Gan-Or Z, International Parkinson's Disease Genomic C. Genetic variability and potential effects on clinical trial outcomes: perspectives in Parkinson's disease. J Med Genet. 2020;57(5):331–8

[9]. Marras C, Beck JC, Bower JH, Roberts E, Ritz B, Ross GW, et al. Prevalence of Parkinson's disease across North America. NPJ Parkinsons Dis. 2018; 4:21.

[10]. Postuma RB, Iranzo A, Hu M, Hogl B, Boeve BF, Manni R, et al. Risk and

predictors of dementia and parkinsonism in idiopathic REM sleep behaviour disorder: a multicentre study. Brain. 2019;142(3):744–59.

[11]. Reeve A, Simcox E, Turnbull D. Ageing and Parkinson's disease: why is advancing age the biggest risk factor? Ageing Res Rev. 2014; 14:19–30.

[12]. Schapira AHV, Chaudhuri KR, Jenner P. Non-motor features of Parkinson disease. Nat Rev Neurosci. 2017;18(8):509.

[13]. Spillantini MG, Schmidt ML, Lee VM, Trojanowski JQ, Jakes R, Goedert M. Alpha-synuclein in Lewy bodies. Nature. 1997;388(6645):839–40.

[14]. Verstraeten A, Theuns J, Van Broeckhoven C. Progress in unraveling the genetic etiology of Parkinson disease in a genomic era. Trends Genet. 2015; 31(3):140–9.

[15]. von Linstow CU, DeLano-Taylor M, Kordower JH, Brundin P. Does developmental variability in the number of midbrain dopamine neurons affect individual risk for sporadic Parkinson's disease? J Parkinsons Dis. 2020; 10(2):405–11.

[16]. Carnino JM, Lee H, Jin Y. Isolation and characterization of extracellular vesicles from Broncho- alveolar lavage fluid: a review and comparison of different methods. Respir Res. (2019) 20:240. Doi: 10.1186/s12931-019-1210-z

[17]. Salimi L, Akbari A, Jabbari N, Mojarad B, Vahhabi A, Szafert S, et al. Synergies in exosomes and autophagy pathways for cellular homeostasis and metastasis of tumor cells. Cell Biosci. (2020) 10:64. Doi: 10.1186/s13578-020-00426-y

[18]. Babaei M, Rezaie J. Application of stem cell-derived exosomes in ischemic diseases: opportunity and limitations. J Transl Med. (2021) 19:196. Doi: 10.1186/s12967-021-02863-w

[19]. Doyle LM, Wang MZ. Overview of extracellular vesicles, their origin, composition, purpose, and methods for exosome isolation and analysis. Cells. (2019) 6: e128060. Doi: 10.3390/cells8070727

[20]. Van Niel G, D'angelo G, Raposo G. Shedding light on the cell biology of extracellular vesicles. Nat Rev Mol Cell Biol. (2018) 19:213–28. Doi: 10.1038/nrm.2017.125

[21]. Mansouri N, Willis GR, Fernandez-Gonzalez A, Reis M, Nassiri S, Mitsialis SA, et al. Mesenchymal stromal cell exosomes prevent and revert experimental pulmonary fibrosis through modulation of monocyte phenotypes. JCI Insight. (2019) 4: jcs222406. Doi: 10.1172/jci.insight.128060

[22]. Soekmadji C, Hill AF, Wauben MH, Buzas EI, Di Vizio D, Gardiner C, et al. Towards mechanisms and standardization in extracellular vesicle and extracellular RNA studies: results of a worldwide survey. J Extracell Vesicles. (2018) 7:1535745. Doi: 10.1080/20013078.2018.15 35745

[23]. Thery C, Witwer KW, Aikawa E, Alcaraz MJ, Anderson JD, Andriantsitohaina R, et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. J Extracell Vesicles. (2018) 7:1535750. Doi: 10.1080/20013078.2018.1535750

[24]. Latifkar A, Hur YH, Sanchez JC, Cerione RA, Antonyak MA. New insights into extracellular vesicle biogenesis and function. J Cell Sci. (2019) 132: jcs222406. Doi: 10.1242/jcs.222406

[25]. Carnino JM, Ni K, Jin Y. Post-translational modification regulates formation and cargo-loading of extracellular vesicles. Front Immunol. (2020) 11:948. Doi: 10.3389/fimmu.2020.00948

[26]. Poulet G, Massias J, Taly V. Liquid biopsy: general concepts. Acta Cytol. (2019) 63:449–55. Doi: 10.1159/000499337

[27]. Mulcahy LA, Pink RC, Carter DR. Routes and mechanisms of extracellular vesicle uptake. J Extracell Vesicles. (2014) 3. Doi: 10.3402/jev. v3.24641

[28]. Carnino JM, Lee H, He X, Groot M, Jin Y. Extracellular vesicle-cargo Mir185-5p reflects type II alveolar cell death after oxidative stress. Cell Death Discov. (2020) 6:82. Doi: 10.1038/s41420-020-00317-8

[29]. Zhang D, Lee H, Jin Y. Delivery of functional small rnas via extracellular vesicles in vitro and in vivo. Methods Mol Biol. (2020) 2115:107– 17. Doi: 10.1007/978-1-0716-0290-4_6

[30]. Shang M, Ji JS, Song C, Gao BJ, Jin JG, Kuo WP, et al. Extracellular vesicles: a brief overview and its role in precision medicine.

Methods Mol Biol. (2017) 1660:1–14. Doi: 10.1007/978-1-4939-7253-1_1

[31]. Kou L, Bhutia YD, Yao Q, et al. Transporter-guided delivery of nanoparticles to improve drug permeation across cellular barriers and drug exposure to selective cell types. Front Pharmacol. 2018; 9:27.

[32]. Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015;33(9):941-951.

[33]. Mitragotri S, Lammers T, Bae YH, et al. Drug delivery research for the future: Expanding the nano horizons and beyond. J Control Release. 2017; 246:183-184

[34]. Mitchell MJ, Billingsley MM, Haley RM, et al. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2021;20(2):101-124.

[35]. Sercombe L, Veerati T, Moheimani F, et al. Advances and challenges of liposome assisted drug delivery. Front Pharmacol. 2015; 6:286.

[36]. Anselmo AC, Mitragotri S. Nanoparticles in the clinic: an update. BioengTransl Med. 2019;4(3): e10143.

[37]. Caliceti P, Matricardi P. Advances in drug delivery and biomaterials: Facts and vision. Pharmaceutics. 2019;11(1):48.

[38]. Teymouri M, Mashreghi M, Saburi E, et al. The trip of a drug inside the body: From a lipid-based nanocarrier to a target cell. J Control Release. 2019; 309:59-71.

[39]. Lalloz A, Bolzinger MA, Faivre J, et al. Effect of surface chemistry of polymeric nanoparticles on cutaneous penetration of cholecalciferol. Int J Pharm. 2018;553(1-2):120-131.

[40]. Wang SJ, Huang WS, Chuang CM, et al. A phase 0 study of the pharmacokinetics, biodistribution, and dosimetry of 188Re-liposome in patients with metastatic tumors. EJNMMI Res. 2019;9(1):46.