

Nanotechnology; Its Application, Process Development And Nano-Technology Based Herbal Medicine

Ms. Pooja S Murkute¹, Mr. Nakul P Kathar², Dr. Gajanan S Sanap³

Department of Pharmacognosy: Late Bhagirathi Yashwantrao Pathrikar College of D. Pharmacy (B. Pharm & D. Pharm), Department of Pharmaceutics: Late Bhagirathi Yashwantrao Pathrikar College of D. Pharmacy (B. Pharm & D. Pharm)

Corresponding Author: Ms. Pooja S Murkute

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ABSTRACT

Nanotechnology is playing vital role in major lethal diseases like Cancer, Heart attack, Alzheimer's disease, serious inflammatory or infectious diseases. Nanotechnology is science of Nano size particles. Nano size particles are included in size range of 10-1000 nm. Nano size particles are divided into organic & Inorganic Nano carrier / Nanoparticles, which include liposomes, Polymeric nanoparticles, Dendrimer, Carbon nanocomposites, Nanospores etc. The nanotechnology have many advantages by focus on inorganic nanostructure material that acquires good antibacterial property. So nanotechnology is emerging science it uses synthetic as well as herbal Nano formulation against various disease condition. Reported evidence of herbal medicinal plant is found in ancient time. As it is reported herbal medicine is not having any side effect, this property is implemented into nanotechnology and it is used against various diseases, so there are no of Nanotechnology medicine which is formulated with the combination of Herbs or traditional medicinal plant and Nanotechnology like Curcuminoids base Solid-Liquid Nanoparticle, Artemisinin based Nanocapsules etc. Nanomedicines were formulated by using various processes like hot homogenization, Ultrasonication, Electrospinning etc. Nanomedicines were analyzed by various nanotechnology tools available into the market.

KEYWORDS: Nanotechnology, Nanocarriers, Organic-Inorganic Nanoparticle, Hot-Homogenization Atomic Force Microscopy, Herbal Nano-Medicine

I. INTRODUCTION

Nanomedicines are known to be nanoentities whose size ranges from 10 to 1000 nm [20]. Trending method for drug delivery is known by more frequent administrations [45]. With the help

of novel drug delivery system like solid dispersion, microemulsion, nanoemulsion & nanoparticle the recent pharmaceutical research is able to solve the scientific needs [22, 29]. Variable no of nanocarrier system such as polymeric micelles, liquid crystal, solid lipid nanoparticles (SLNs), precursors systems for liquid crystals (PSLCs), liposomes and micro emulsions, have tried to break this barrier; to be used in formulations and even change the substances property. They allow substances with different properties to be used in same formulation and even alter substance properties and behavior in a living environment. These technical discoveries have revolutionized drug delivery [46].

The new modern drug delivery substance have ability to enhance the effectiveness of active constituent as well as the reintroduction of compound which was discarded because of their least activity. Moreover, the activity of latest substances has been increased, like by reducing side effect, protecting against photo-degradation, efficacy & selectivity and by controlling the discharge of active constituents [19, 35, 46]. Various Pharmaceutical company have become interested in nano technological advances because these system provide various advantage such as modified release systems and the ability to develop new formulations that were previously not possible because of certain active component [31]. The use of nanobioscience technology to plant extractions product has been cited widely in literature, because Nano carrier has ability to increase the activity of plant extraction product which reduce the necessary dose, promoting sustained release of active ingredient, lower side effects and improve activity [16, 40]. The Nano carrier system can efficiently enhance the therapeutic index and pharmacokinetics of crude drugs. Target site delivery and combinational therapy can drastically enhance performance of crude drug [30]. Till now the biologists have succeeded in using this

technology to introduce DNA to tobacco and corn plants that is recombinant DNA technology researchers are capable to incorporate several substances into the plants at one time and release them in a time sustained release manner. Nano system is having ability to penetrate into the cell wall of the plant which enables biologists to view plant physiology [25].

a. APPLICATION OF NANOTECHNOLOGY

1. Hyperthermic cancer therapy and imaging is possible with combined hard and soft magnetic property [48].
2. The nano scale imaging approached design to probe molecular mechanisms in living cells is the significance of this research which lies in the development of a platform technology [33].
3. Detection of target cells, gene regulation therapy and expression of green fluorescence protein optically is possible because of MRI with hybrid probe of nanoparticle [9].
4. The nanotechnology with molecular imaging is giving large platform for naval drug delivery system of Nano probe which is responsible to enhance specificity, sensitivity, signaling of nanotechnology with various biomarkers in various diseases [24].
5. The Therapeutic and pharmacological properties of drug can be enhance by proper designing of drug delivery systems with the use of lipid and polymer based Nano particles[3].
6. The nanotechnology has been advanced by focus on inorganic nanostructure material that acquires good antibacterial property [15].

7. Multipurpose nanoparticles are develop that would detect, image and treat tumor in various type of cancer treatment [36].
8. Nano wires are being used to prepare sensor test chips which are helpful in detection of protein and other biomarkers left behind cancer cells and also it is responsible for detection of cancer into human body from single cancer cells. The different nanotechnology based herbal medicines and its method of preparation is mentioned in Table no: I Under heading Nanotechnology based herbal medicines [51].

b. ADVANTAGES OF NANOTECHNOLOGY[29]

1. In Nanotechnology conjugation of semisynthetic origin which is composed of proteins, inorganic nanoparticles and nucleic acids is being synthesize and characterized [37].
2. Nanotechnology with the help of Nano bionics is helpful in solving problems of facing between medical appliances and the nervous system [47].

c. DISADVANTAGES OF NANOTECHNOLOGY

1. There may be chance of major health risk due to small particle size nanocarrier which may lead to allergic reaction. Around 60 seconds of nanocarrier inhalation of nanoparticle may lead to damage lung easily [38].
2. Organic / Inorganic chemicals biosensors with composition of DNA Wrapped CeO₂ nanorods showed some interfering responses with other anions [6].

NANOTECHNOLOGY BASED HERBAL MEDICINES

ACTIVE INGREDIENT	NANO FORMULATION	METHOD OF PREPARATION	REFERENCE
Curcuminoids	Curcuminoids base Solid-Liquid Nanoparticle	Micro-emulsion technique	[49]
Artemisinin	Artemisinin based Nanocapsules	Self-Assembly method	[49]
Glycyrrhizin acid	Glycyrrhizin Acid loaded Nanoparticles	Rotary-Evaporated Film and Ultrasonication Method	[42]
Flavonoids and Lignans	Cuscuta chinensis based nanoparticles	Nanosuspension Method	[49]
Berberine	Berberine Loaded nanoparticles	Self assembly method	[49]

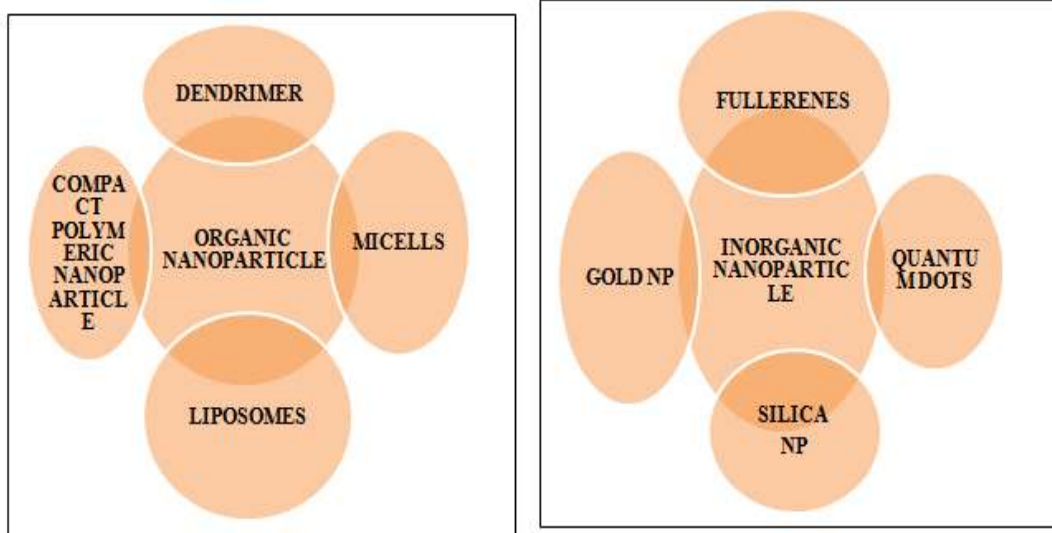
Taxal	Taxal Loaded Nanoparticles	Emulsion Solvent Extraction Method	[49]
Curcumin	Diclofenac diethylamine and curcumin loaded nanoparticles.	Encapsulation with sonication	[8]
Curcumin	Nanotrasformers of curcumin and diclofenac diethylamine	Encapsulation with sonication	[7]
Curcumin	Curcumin loaded NP of HPMC and PVP	Solvent emulsion-evaporation technique	[10]
Quercetin	Quercetin SNEDDS formulation	Self nanoemulsion method	[2]
Cysteine which residues in protein	AgNPs of Mukia scabrella	Nanosuspension method	[2]
Amides and phenolics	Fluorescent AgNPs of Artemisia annua	Nanosuspension method	[27]
Curcumin	NPs loaded (PH Sensitive) curcumin-celecoxib combination	Solvent emulsion Evaporation	[39]
Amines, amides, phenolics and alcoholic	AuNPs of Pisticia intergerrima gall extract	Nanosuspension method and Sonication	[23]
Curcumin and temozolomide	Curcumin and temozolomide loaded magnetic NP's	Nanosuspension with Sonication	[12]
Gallic, Chlorogec, caffeic and ellagic acid, catechin, epicatechin, quercetin	Polymeric NP formulation of Syzygium cumini	Emulsification or Evaporative Technique	[5]
Essential oil	SNEDDS formulation of Zedoary turmeric oil	Self nanoemulsion	[50]
Cinnamon oil	Cinnamon oil microemulsion	Self nanoemulsion	[16]
5,7-Dihydroxy-6-methyl-8-prenylflavanone	Insertion of four prenylated flavanones from Eysenhardtia platycarpa leaves	Oil, solvent and surfactant cosurfactant mixture	[13]

Table no 1: Nanotechnology based herbal medicines

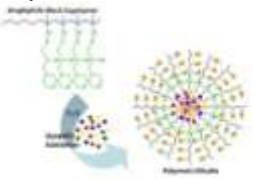
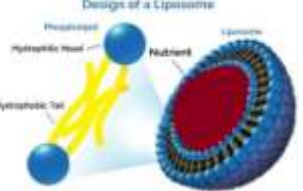

II. VARIOUS NANOCARRIERS/NAOPARTICLE

Based on application and method of treatment i.e. diagnosis, imaging tumor therapy there are different types of Nanocarrier system have been proposed [19, 40, and 42]. These nanocarrier types are divided in two main groups: Organic and Inorganic Nanocarrier system. The

first group i.e. organic nanocarrier system includes micelles, dendrimers, liposomes, hybrid and compact polymeric Nanoparticles. The second group i.e. inorganic nanocarrier system includes fullerenes, quantum dots, silica and gold NPs. The different types nanoparticles is mentioned following under heading Types of nanoparticles



TYPES OF NANOCARRIERS

TYPES OF NANOPARTICLES	DEFINATION
<p>Polymeric micelles</p>  <p>Figure no 7</p>	<p>Polymeric Micelles are nanocarrier made up of amphiphilic molecules like polymers or lipids [42].</p>
<p>Liposomes</p>  <p>Figure no 8</p>	<p>Liposomes are vesicles in nature & made entirely of lipidic compounds. The most common are the unilamellar liposomes whose size usually ranges from 100 to 800 nm [41].</p>
<p>Dendrimers</p>  <p>Figure no 9</p>	<p>A dendrimer is morphologically characterized by a branched structure extended from one or more cores [42].</p>

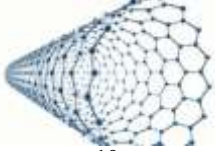
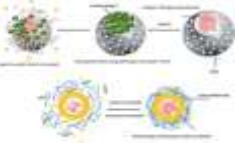
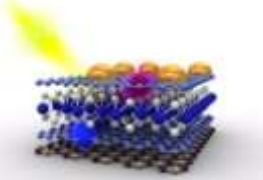
<p>Carbon nanoparticles</p>  <p>Figure no 10</p>	<p>Carbon nanoparticles are surface functional molecule with organic molecule or polymeric in nature which binds to the surface boundary.</p>
<p>Silica nanoparticles</p>  <p>Figure no 11</p>	<p>It has great potentials in protein separation and adsorption, nucleic acid detection, drug and gene delivery and bio imaging [35].</p>
<p>Nanocomposites</p>  <p>Figure no 12</p>	<p>Nanocomposites are materials that include Nano sized particles into a matrix of standard material.</p>

Table no 2: Various nanocarriers / nanoparticle

III. PROCESS DEVELOPMENT OF NANOTECHNOLOGY BASED HERBAL MEDICINE

For the formulation of nanotechnology based Nano product there is various methods which are used for the development of the Nano formulation. Specifically these methods are developed based on different nanocarrier system. The main feature of these methods is reduction of particle size and also the uniformity in formulation product.

a. NANO SPRAY DRYERS

Nano spray dryer's deals with victimization spray drying to form particles within the nanometers. Spray drying may be a mild methodology for manufacturing powders with a micro particle size for emulsion, suspension and

dispersion that is widely used for prescription of drugs, biotechnology and other industrial use. In the past, the restrictions of spray drying were the particle size (minimum a pair of micrometers), the yield (maximum around 70%), and also the sample volume (minimum 50 ml for appliances in laboratory scale). Recently, minimum particle sizes are reduced to three hundred nm, yields up to ninetieth square measure doable, and also the sample quantity may be as tiny as one milliliter. These distended limits square measure doable new technological developments to the spray head, the heat, and also the static particle collector. To emphasize the little particle sizes feasible with this new technology, it's been named as "Nano spray drying". However, small particles produce in sub micrometer are similar to fine particles [17].

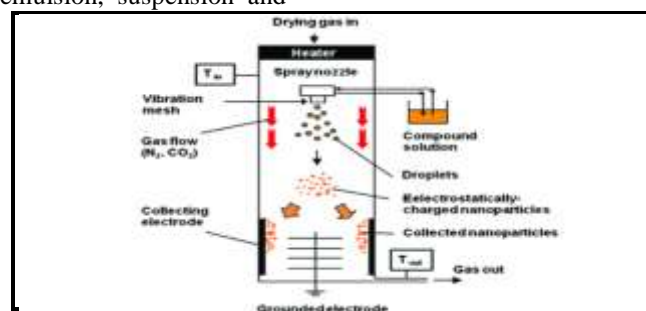


Figure no 1: Nano spray dryers: The process development

b. ELECTROSPINNING

It is fiber production technique that uses electrical force to arrange charged threads of compound solutions. It gives specification each electrospinning and traditional resolution dry spinning of fibers [20]. The process does not need the utilization of curdling chemical synthesis or temperatures to supply solid threads from resolution. This makes the method significantly suited to the assembly of fibers exploitation massive and complicated molecules.

Electrospinning from liquefied precursors is additionally practiced; this technique confirms that solvents are not supplied inside the ultimate product. The Electrospinning consists of hypodermic needle in standard laboratory setup which is attached to syringe pump, high-voltage (5 to fifty kV) electricity power and collector. A compound resolution particulate suspension, sol-gel or soften is filled into injection and this liquid is removed from needle tip at continuing rate by a syringe pump [34].

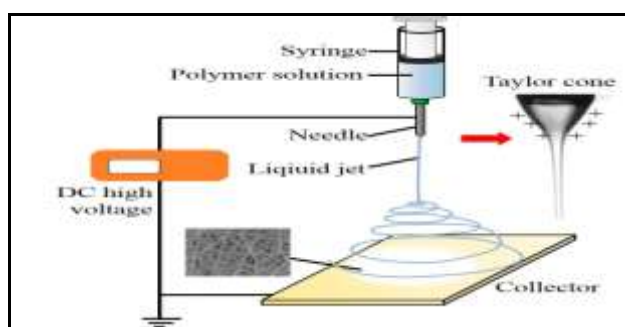


Figure no 2: Electrospinning: The process development of nanotechnology based herbal formulation

c. HOT-HOMOGENIZATION

In this process drug available in melted position. Then there is dispersion of lipid phase in hot aqueous surfactant mixture than formation of Pre-emulsion with continuous stirring than under

high pressure Homogenization the formation of o/w Nanoemulsion. The prepared nanoemulsion is transferred to process of solidification. After the completion of this process the solid liquid nanoparticles are being produced [34].

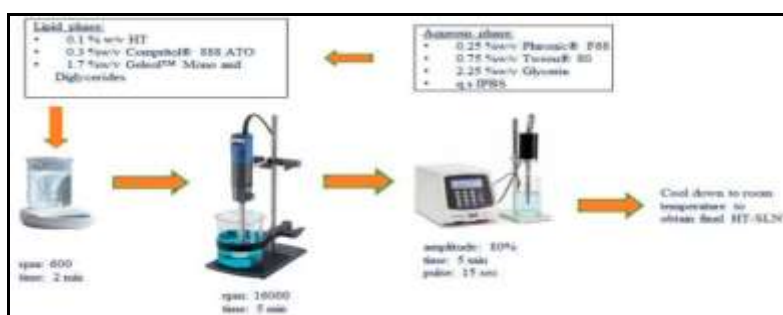


Figure no 3: Hot homogenization: The process development of nanotechnology based herbal formulation.

d. ULTRA-SONICATION

The radiation of liquid with supersonic (>20 kHz) waves leading to agitation. Sound waves transfer into liquid media which results into alternating compression and rarefaction cycles. High-intensity ultrasonic sound waves create void spaces and also small vacuumed bubbles during the concentration, during compression which finally

collapse violently, homogenizers are term as ultrasonic processors, to enhance stability and uniformity the tracer particles a liquid reduces. Disperse phase particles are available in many liquid or solid form. Ultrasonic homogenizing is extremely economical for the reduction of sentimental and laborious particles. Hielscher produces supersonic devices for the grinding of any

liquid volume for inline or batch process. Lab scale ultrasonic devices used for volumes upto 2L. Ultrasonic industrial devices are used for the

process development and production of batches from 0.5 to approx. 2000L or flow rates from 0.1L to 20m³ per hour [49].



Figure no 4: Ultrasonication method: The process development of nanotechnology based herbal formulation

IV. NANOTECHNOLOGY TOOLS

Nanotechnology tools and instruments are the hardware, software which is used to measure and manipulate structures on the nanoscale. Nanotechnology tools include microscopes, probes, lithography systems, manipulation and fabrication systems software and other accessories. There are number of nanotechnology tools available that can be used in process as well as product development. The process development is nothing but synthesis of drugs its drug intermediates and to the development of analytical tools for diagnosis.

- a. Miniaturization
 - b. Atomic force microscopy
 - c. Confocal microscope
 - d. Optical lithography
 - e. Scanning acoustic microscope
- a. Miniaturization and Automation

It is useful in organic chemistry and screening of biological material on nanoscale range. The examples of these tools are the X-cubeTM system and NanoSynTestTM-system. The characteristic feature of these system is to manipulate reaction on Nano-titer plates with density of about 100 wells/cm² and limit is about Nanoliter volume [28].

- b. Atomic Force microscopy
 Atomic Force Microscopy is also known as Scanning Force microscopy. This device use to imaging, visualizing, taking measures and for changing object that are arrange in nanometer scale. The Scanning Tunneling Microscope is developed in 1980 which is earlier version of AFM. Mechanical probe is situated on these device that is use for sensing of material which is place on surface.

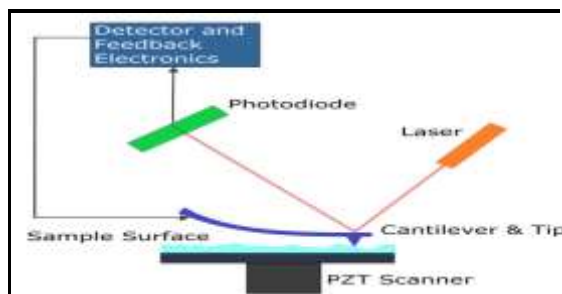


Figure no 5: Atomic Force Microscopy: Nanotechnology tool

- c. Confocal microscope
 Confocal microscope includes a minute light source and detectors are used to observe a fluorescence labeled specimen. Diffraction results into, the illuminating wave front create a 3D

intensity distribution in presence of focal spot. This phenomenon is described physically with the help of point spread function of microscopic objective lenses [21].

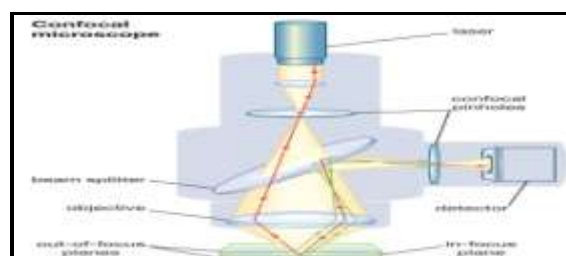


Figure no 6: Confocal Microscope: Nanotechnology tools.

d. Optical lithography

Optical lithography tool become prime important pult - tern description process in microelectronics. It is used for semiconductor devices, integrated circuits, magnetic elements and circuit's thin-film and thick-film passive connections and packaging. Additionally, it is used to create chrome masks for itself md patterns for other technologies such as silk screen printing and mask-delineated evaporation. It has participated in a vast way to the vast increases in productivity in electronics over the past decade[11].

started to explore the potential of such associate instrument and compare its performance therewith of the optical version. The acoustic microscope would provide us with a new method for delineating the detail of microscopic objects if it could be made with a resolution comparable to the optical instrument. 1 In principle this can be done. With a frequencyof 1 GHz the wavelength for sound in water is near 15 /J.m. The utility of such an instrument arises because the disperse of acoustic waves is dependent on the change in elastic properties, whereas it is the change in the index that determines the scattering of optical waves [32].

e. Scanning Acoustic Microscope

A magnifier are often created with acoustic waves instead of optical waves. We have

V. COMPARATIVE STUDY OF TRADITIONAL V/S NANOMEDICINES

ACTIVE INGREDIENT	TRADITIONAL MEDICINE	NANO MEDICINE	REFERENCE
Zingerol	Gingerol decoction for respiratory infection	Phytosome complexed with chitosan for gingerol delivery to treat respiratory infection: In vitro and in vivo evaluation	[43]
Liquorice	Licorice extract cream	18β-glycyrrheticin Acid Nano-Rods Atopic dermatitis with licorice gel	[1]
Ashwagandha	Herbal formulation (capsule) containing As a single herb with their nutritional value	Ashwagandha Phytosomes Capsule its formulation and evaluation	[26]
Achyranthine	A decoction of the whole plant of A.	Gold nanoparticles of plant Achyranthes	[44]

	aspera	aspera herbal medicine which is significance in leprosy	
Quinine	Quinine Sulphate 300mg Coated Tablets	Quinine loaded nanocapsules of malaria treatment	[18]
Neolignans	Myristica fragrans Extract.	Silver nanoparticles using Myristica fragrans seed (nutmeg) extract for typhoid	[4]

Table no 3: Comparative study of traditional v/s nanomedicine

VI. NANOTECHNOLOGY BASED PRODUCT SURVEY [14]

YEAR (FDA APPROVAL)	NANO PRODUCT (BRAND NAME)	USES
1955	Ritalin	It is used in Hyperreactivity problem
1957	Thalidomide	This medication is used to treat or prevent certain skin conditions related to Hansen's disease,
1965	Abelcet	Used for treatment of serious leishmaniasis and fungal infection such as Aspergillosis ,Blastomycosis, Candida
1990	Adagen	It is useful in Bone marrow transplants and transfusion of frozen irradiated erythrocytes
1994	Oncaspar	Treat acute lymphoblastic leukemia, and chronic myelogenous leukemia.
1995	Doxil	Extensively used for Cancer therapy.
1996	Daunoxome	It is used in case of Cancer & HIV associated kaposi sarcoma.
2000	Renagel	Prescribed for cases of end-stage renal disease.
2001	Visudyne	For treatment of choroidal neovascularization
2002	Neulasta	Neulasta is used for the treatment of consequent infections & febrile neutropenia.
2002	Pegasys	It is used for Hepatitis C and hepatitis B.
2002	Eligard	It is used in Prostate cancer therapy.
2003	Emend	It is acting as Antiemetic drug.

2003	Vitoss	It has ability to Mimic structure of cancellous bone.
2003	Somavert	Treatment of acromegaly, Somavert is an antagonist of GH receptors, blocking the binding of GH.
2003	Estrasorb	It is used for Moderate vasomotor symptoms due to menopause.
2004	Ostim	It is used for Orthopedic & dental Surgery.
2004	Tricor	Decrease level of Triglyceride & cholesterol for to prevent atherosclerosis.
2004	Macugew	It is used in various problem like age-related macular degeneration.
2007	Mircera	It is used for treatment of Anemia.
2007	Depocyte	It is useful in case of lymphomatous meningitis.
2008	Cimzia	It is used in case of Patients with rheumatoid arthritis, Crohn's disease, psoriatic arthritis and ankylosing spondylitis.
2010	Rapamane	For Prevention of rejection of kidney transplantation.
2010	Krystexxa	It is used for Tophaceous gout disorder.
2012	Abraxane	It is used for treatment of breast cancer.
2017	Vyxeos	It is used for treatment of acute myeloid leukemia.
2017	Zilretta	It is used for treatment of osteoarthritis.
2017	Rebinyn	It is useful in the treatment of hemophilia.
2018	ONPATPRO	To treat nerve problems due to a certain inherited condition
2019	NBTXR3	Locally advanced soft tissue sarcoma

Table no 4: Nanotechnology based product survey

VII. CONCLUSION

Above mention topic particularly emphasis on Herbal Nanomedicine product, as different synthetic formulations are having number of adverse effect but the Nano formulations prepared by Herbal ingredient is giving minimum side/adverse effect. The Introduction, Nanocarrier classification, Comparative study of different traditional v/s Nanomedicines are also mentioned in this topic. The application in different area, advantages & disadvantages are also discuss in this topic. Nanotechnology is the emerging science were different Nano carriers classification gives the Idea about different area and way of design, and

formulation of Nanomedicine which enhance delivery of poorly water soluble herbal drugs. Nanotechnology tools available that can be used in process as well as product development.

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