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A REVIEW ON TREATMENT OF CANCER BY NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

Cancer is one of the most fatal diseases in all over the world. Due to which, many countries trying to implement various curable treatments for decades. Since last 20th century new improved methods and treatments were developed like chemotherapy and radiation therapy, which gives an effective result along with surgery. Medicines are also imparted with newly modern changes called as novel drugs and novel drug delivery system (NDDS). Novel drug delivery system (NDDS) is a new approach to gives improved form of medications with its therapeutic effects. This delivery system ease the overall treatment by providing targeted action, controlled release of active pharmaceutical ingredients with maintaining systemic circulations and enhance drugs therapeutic effects with dosage. It includes Microsphere, Nanoparticle, Dendrimer, Liposome, Niosome and Ethosome type of delivery system.

Keywords: -
Cancer, Novel drug delivery system (NDDS), Nanoparticle, Microsphere, Liposome, Niosome.

INTRODUCTION

Cancer is one of the complex structural diseases, happens by genetic modification which leads to the abnormal transformation of normal cells into cancerous tumours. Cancer mainly arises due to gene mutation causes uncontrolled growth of normal cells and leads to abnormal cell division and forms tumours, which spreads to other parts of the body [1]. Cancer is the result of collection of abnormalities of genes and genetics and epigenetic modifications [2]. Cancers are identified by uncontrolled growth of cells due to removal of control on important proteins and enzymes which are responsible for cell division and proliferation [3]. The main causes of cancer disease involves uncontrolled and excess use of drugs for long time, among which the most common cause called as nicotine dependence by using of tobacco containing products like (cigarette, cigar, pipe smoke etc.) they generally causes mouth cancer and lung cancer, excess using of alcohol increases the risk of cancers like (mouth, breast, bowel, pharyngeal cancer etc.), by infectious organisms and viruses like (papilloma virus, hepatitis B and hepatitis C virus etc.) , by improper unhealthy diet, by carcinogens and environmental toxins, hormone and immune conditions which ultimately contribute to cause cancer [4].

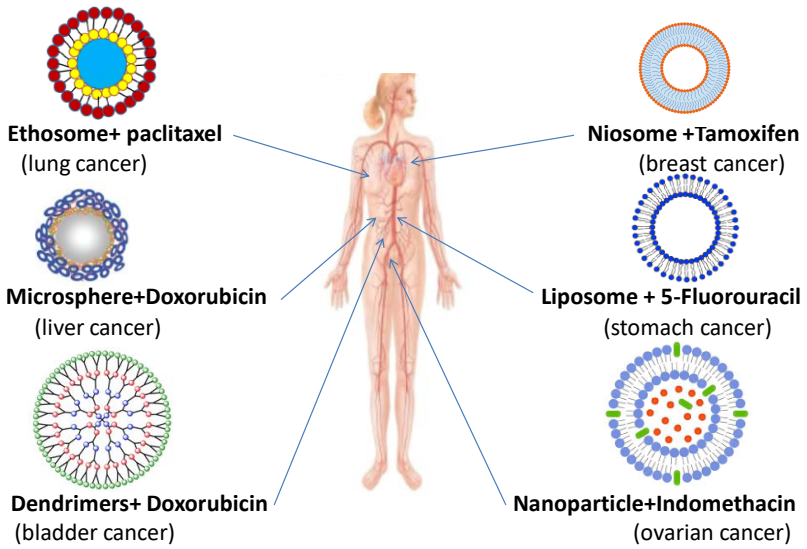

Fig 1: - Novel Drug Delivery System acting on Cancer.

Anticancer agents

Anticancer also called as anti-neoplastic agents, which are used to treat, prevent the development of cancer or inhibit the growth of malignant cancerous cells or tumours [5]. Anticancer drugs are categorized according to their mechanism of action as antimetabolites, purine and pyrimidine antagonists, an antibiotics, monoclonal antibodies, plant derivatives, biological agents, alkylating agents and hormonal agents [6].

Anticancer therapy

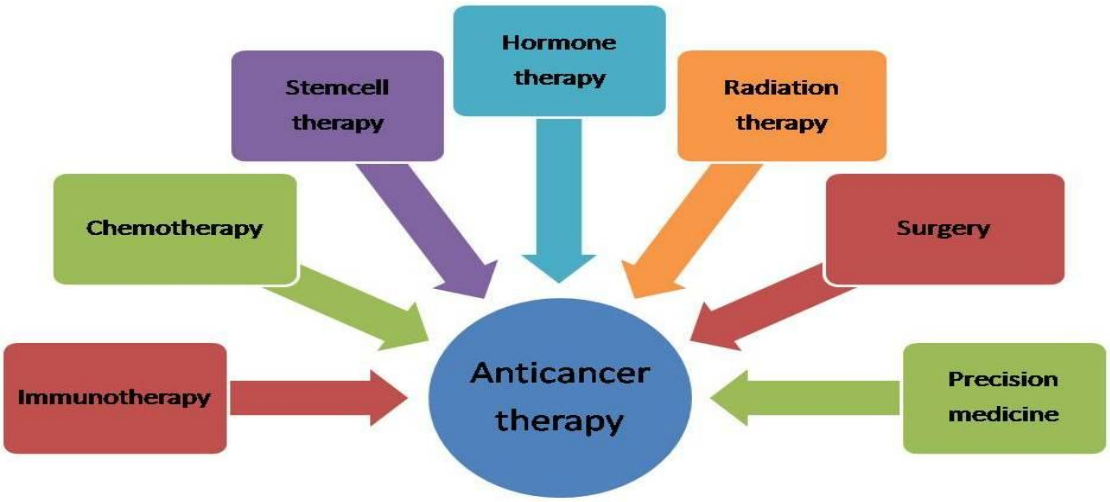

Fig 2: - Different types of Anticancer Therapy.

One of the challenging target or goal in the cancer treatment is the proper removal of tumours from the body without any damage. The main strategy of this treatment is the selection of therapy according to the stage of cancer and tumour's size. The treatment of cancer consists a combination of therapies, including surgery, chemotherapy, radiation therapy, and immunotherapy etc. The main purpose of all the treatment is to destroy the tumour cells to achieve tumour reduction without damaging normal cells [8].

1. Chemotherapy

In chemotherapy, anticancer drugs alone or with combinations are used to inhibit the growth or division of cancerous cells, it is known as the primary treatment and works on whole body also targets normal heathy cells and it is also a painful treatment [9]. Chemotherapy is a commonly used treatment in cancer in which a variety of drugs are usedthat reach almost all the body parts and in tissues and exert its action in both

malignant and normal cells which leads to create various types of adverse effects includes anaemia,fatigue, nausea and vomiting, hair loss, infertility etc [10].

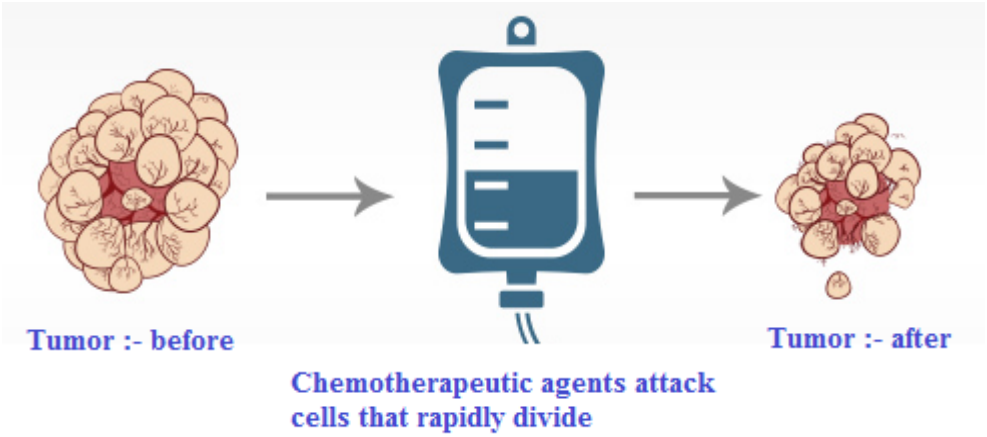

Fig 3: - Chemotherapy in the Treatment of Cancer

2. Immunotherapy

Immunotherapy is mainly used treatment to restore the immune system of the whole body to fight against disease; it improves the natural defence system of the body .the main important checkpoint of immunotherapy is the adaptive immune system in cancer elimination [11]. The adaptive immune system comprises lymphocytes, both T-cells and B-cells, B-cells are involved in humoral immune response whereas T-cells involved in cell mediated immune responses. Both the cells have ability to compete immunogenic cancer [12].

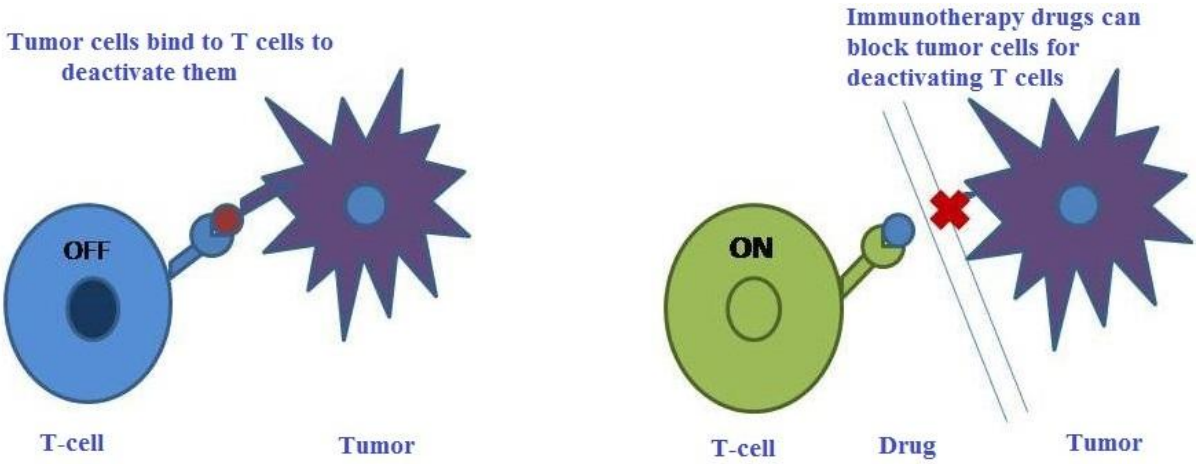

Fig 4: - Immunotherapy in the Treatment of Cancer

3. Radiation therapy

Radiotherapy treatment uses high dose radiations to control or kill, slowing the growth or shrinking of cancerous cells [13]. Radiotherapy mainly consists of two therapies – tele therapy and brachy therapy [14].

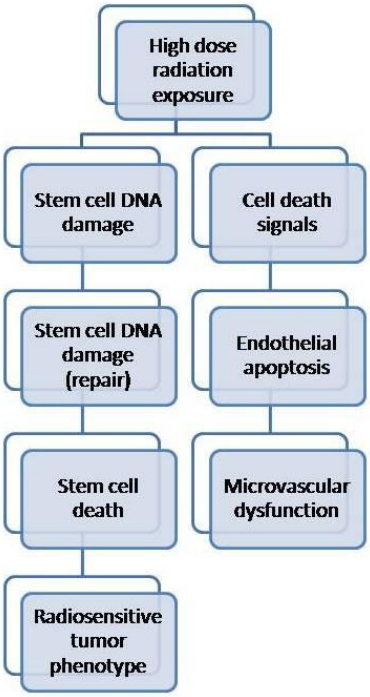

Fig 5: - Radiation Therapy in the Treatment of Cancer

4. Hormone therapy

Hormone therapy mainly uses hormones to treat and fight against cancer. Generally in breast cancer, hormone therapy shows great effectiveness along in combination with another therapies [15].

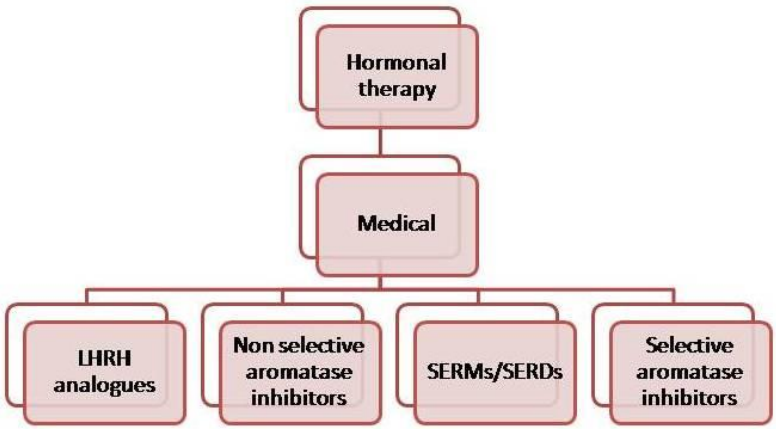

Fig 6: - Hormonal Therapy in the Treatment of Cancer

5. Stem cell therapy

Stem cell therapy is the use of original cells of human beings to cure cancer. Stem cells have the ability/ potential to repair the damaged cells of the body [16]. Cancer stem cells (CSCs) is a portion of tumour cells which have a potential of cell death, renewing cells and proliferative ability [17]. In other words, they have a capacity of regenerating cells and with increasing numbers. This was first documented by Bonnet and Dick [18].

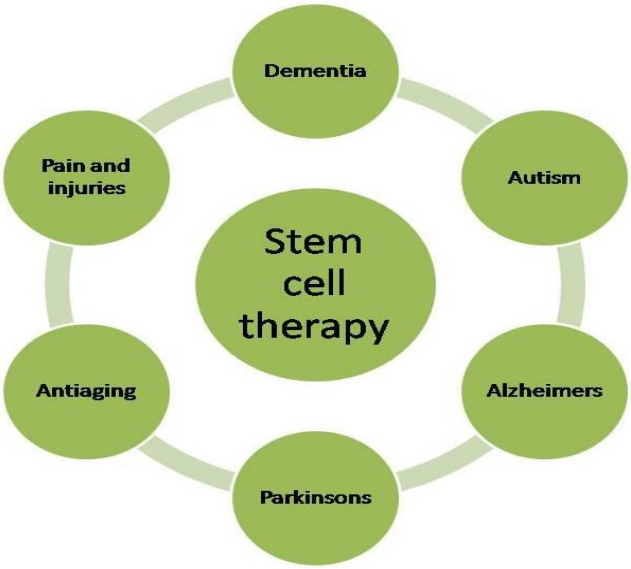

Fig 7:- Stem cell Therapy in the Treatment of Cancer

6. Surgery

In cancer surgery, the cancerous cells or tumours are totally removed or cut out from the body to prevent spreading of tumour cells in the whole body. The only curative treatment for CRC is primary surgical removal [19].

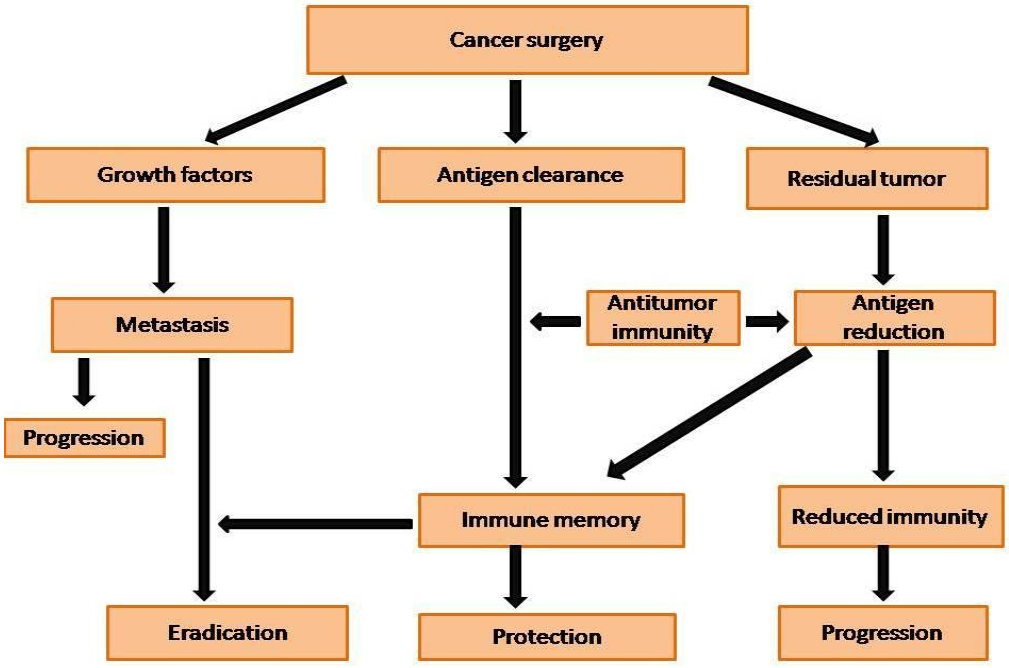

Fig 8: - Surgery in the Treatment of Cancer

7. Precision Medicine

Precision medicines are the treatment through which specific diseases are treated according to individual's patient disease stage [20].

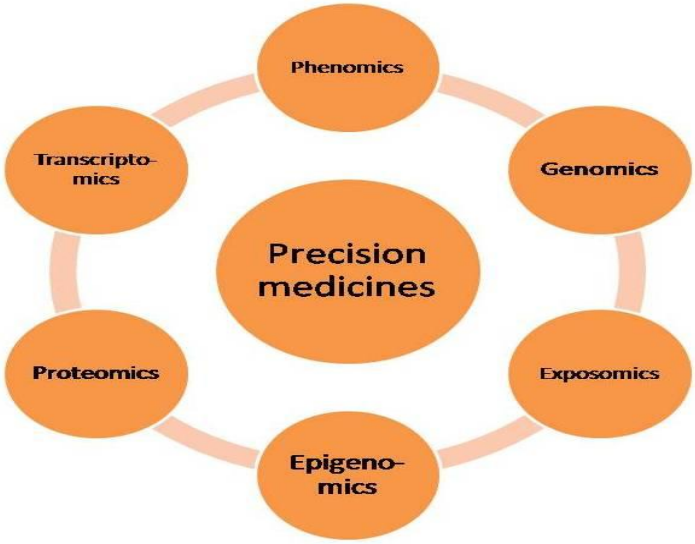

Fig: - 9 Precision Medicines used in the Treatment of Cancer

NOVEL DRUG DELIEVRY SYSTEM

Novel drug refers to new, innovative or improved forms of drugs as compared to existing drugs. Novel drugs are differing from existing drugs by their improved therapeutic efficacy, complete bioavailability, fast action, which also improves patient compliance. Novel drug delivery system is an advanced technique of delivering medicines [21].

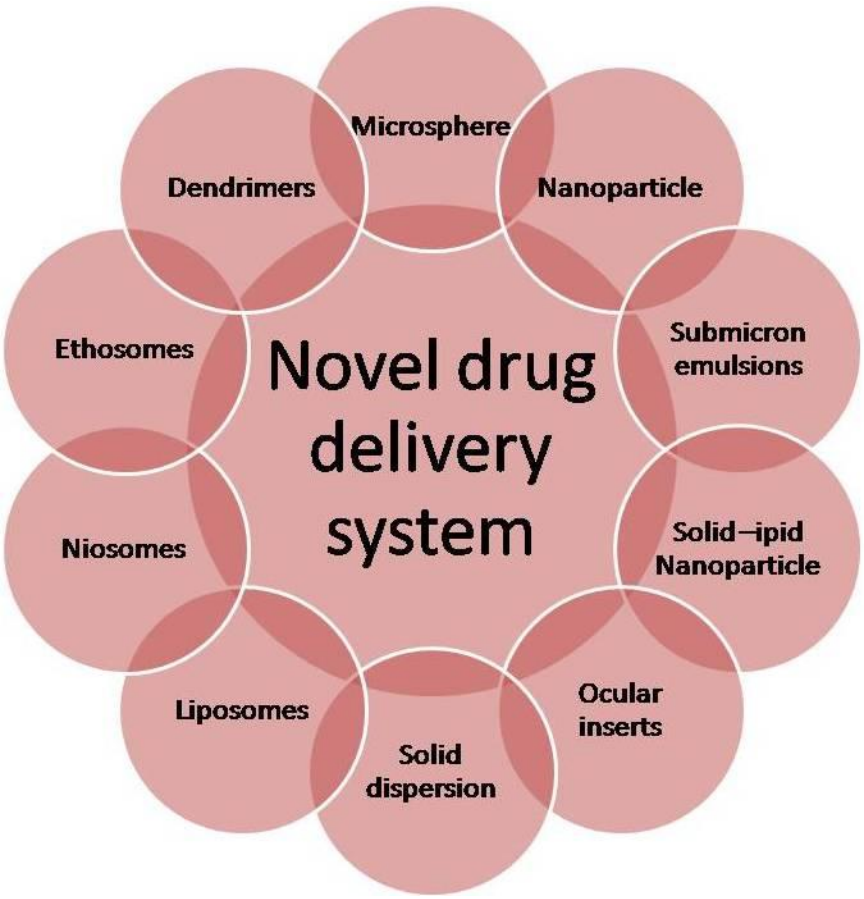

Fig 10: - Different Types of Novel Drug Delivery System.

Novel drug delivery system is an advanced approach which is mainly designed to improve or alter the behaviour of active pharmaceutical ingredients [22]. It improves the physiological condition of the drugs to ease the proper distribution of medicines with desired efficacy and also minimize the drug loss or its degradation [23]. Novel drug delivery system are mainly used to enhance the therapeutic effect of any drug by providing a better physiological conditions, controlling drug release, maintaining systemic circulation, an their site of action [24]. Novel drug delivery system includes

1. Microspheres

Microspheres, also called as microparticles are hollow spheres [25]. Mainly made up of proteins or various synthetic polymers, to enhance the stability property of the drugs that can easily degraded in the body [26].

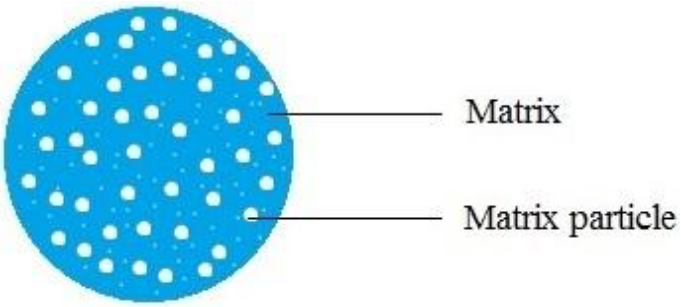

Fig 11: -Microsphere

Table 1: Example of Microspheres used in the treatment of cancer:-

S.no	Polymer	Drug	Outcome	Reference
1.	Chitosan, PEG, N-/2-hydroxypropyl methacrylamide.	Doxorubicin	Decreasing the resistance of topoisomerase 2, tumour cells become resistant	27
2.	Polyurethane	Gefitinib	Inhibits the epidermal growth factor receptor btATP binding sites of an enzyme	28
3.	Chitosan	Cisplatin	Kills cancer cells by binding to DNA	29

Table 2: Cited patents of Microsphere in anticancer:-

S.no	Inventor	Current assignee	Topic	Reference
1.	Yan Chen, Bruce Nathaniel Gray	Sirtex Medical ltd	Controlled release preparation of cytotoxic or cytostatic drug	30
2.	jRichard T. Liggins, Philip M. Toleikis, Dechi Guan	Angiotech International AG	Microparticles with high loadings of a Bioactive agent	31
3.	Katsutoshi Inoue, Tsutomu Yamashita, Kazuharu	Tanaka Kikinzoku Kogyo Kk	Antitumor agent containing chitosan microsphere and production there of	32

2. Nanoparticles

nanoparticles are the nano-sized microscopic particles, in which the inner core is the active pharmaceutical ingredient and the drug is surrounded by a layer of polymer [33]. Nanoparticles behave as a whole body [34].

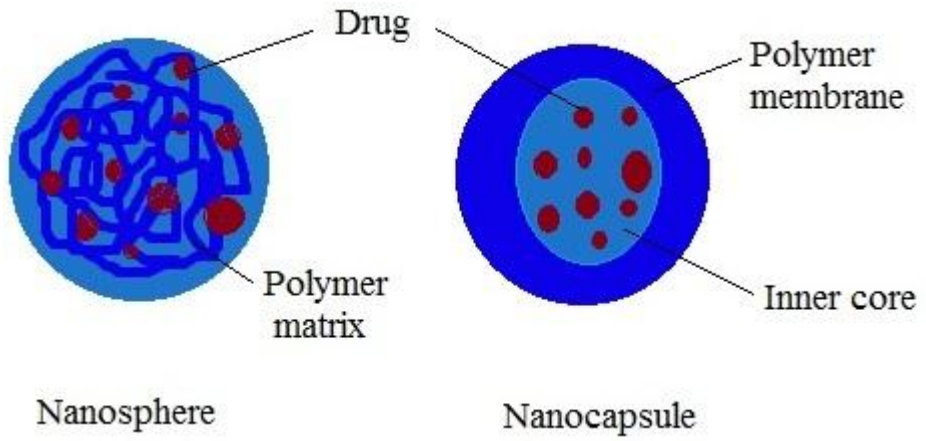

Fig 12:- Nanoparticles

Table 3: **Examples of Nanoparticles used in the treatment of cancer: -**

S.no	Polymer	Drug	Outcome	Reference
1.	Chitosan oligosaccharide	Indomethacin	Chemosensitizing effect, exhibit enhancement of cytotoxic effect	35
2.	Chitosan hydrochloride/hyaluronic acid	Mitoxantrone	Stability in physiological medium	36

Table 4: Cited patents of Nanoparticles in anticancer: -

S.no	Inventor	Current assignee	Topic	Reference
1.	Ulagaraj Selvaraj, Grey.L.Messing	The penn state research foundation	Synthesisi of drug nanoparticle by spray drying	37
2.	Stephen E.Zele, Miro Mukkaram Ali	Pfizer Inc	Cancer cell targeting using Nanoparticles	38

3. Liposomes

Liposomes are small spherical vesicles made up of phospholipids can be used to enclosed aqueous solutions, nutrients and other pharmaceutical drugs [39]. Liposome is a artificial spherical phospholipid bilayered membrane [40]. Liposomes carry a wide range of importance in drug delivery system due to its stability, biocompatibility and its membrane like property selectivity [41]. On the other hand all hydrophilic, lipophilic, peptides and other aqueous extracts can be encapsulated in phospholipid bilayer of liposome [42].

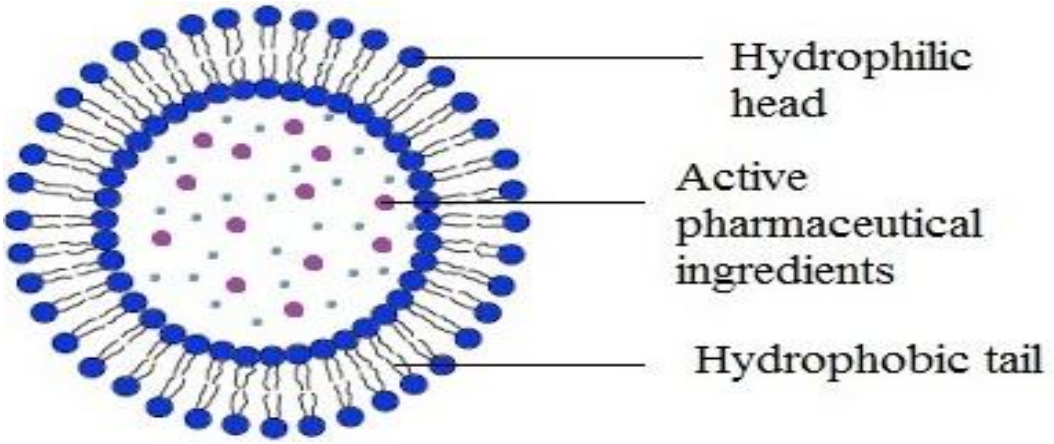

Fig 13:- Liposome

Table 5: Examples of Liposomes used in the treatment of cancer: -

S.no	Polymer	Drug	Outcome	Reference
1.	Dipalmitoyl phosphate-dylcholine	5-fluorouracil	Interference with DNA synthesis and act as a thymidylate synthase inhibitor	43
2.	Alpha tocopherol polyethylene glycol 1000 succinate (TPGS)	Paclitaxel	Improving the solubility and effectively inhibiting p-gp mediated efflux	44

Table 6: Cited patents of Liposome in anticancer drugs: -

S.no	Inventor	Current Assignee	Topic	Reference
1.	Jun Yang, Stephen H.WU, Cliff J. Herman	Mallinckrodt.LLC	Combinational liposome composition for cancer therapy	45
2.	Murali Krishna Divi, George C Wood, M. Waleed Gaber	University of Tennehhee research foundation	Methods and compositions for inhibiting undesirable cellular proliferation by targeted liposome delivery of active agent	46

4. Niosomes

Niosomes are non- ionic surfactant microscopic vesicles consisting of bilayer structure with an an aqueous core [47]. Niosomes were first introduced as a feature of cosmetic industry [48]. Nonionic surfactants are mainly used because of interfacial activity due to which hydrophilicand hydrophobic drugs are entrapped [49].

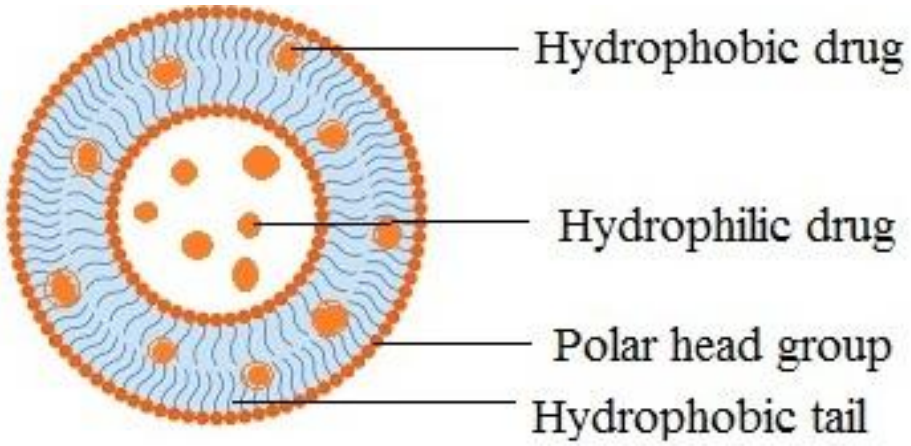

Fig 14 :- Niosome

Table 7: Examples of Niosomes used in the treatment of cancer: -

Polymer	Drug	Outcome	Reference
Poly (methacyclic acid)	Tamoxifen	Modulates the estrogen receptor in breast cancer	50

Table 8: Cited patents of Niosome in anticancer: -

Inventor	Current Assignee	Topic	Reference
Masahiko Ikekita, Taichi Matsunaga, Norimune Nagahara, Isamu Shiina	Tokyo university of science	Anticancer agent containing tamoxifen analogue as active ingredient	51

5. Ethosomes

Ethosomes are the multilayer phospholipid nanovesicles filled with alcohol (20-45%) [52]. Ethosomes differ with liposomes as it can effectively deliver both hydrophilic and lipophilic drugs through the stratum corneum into the deep layer of skin [53]. Hence ethosomes becomes an effective system for skin diseases [54]. It is used in skin related cancers called as melanoma [55].

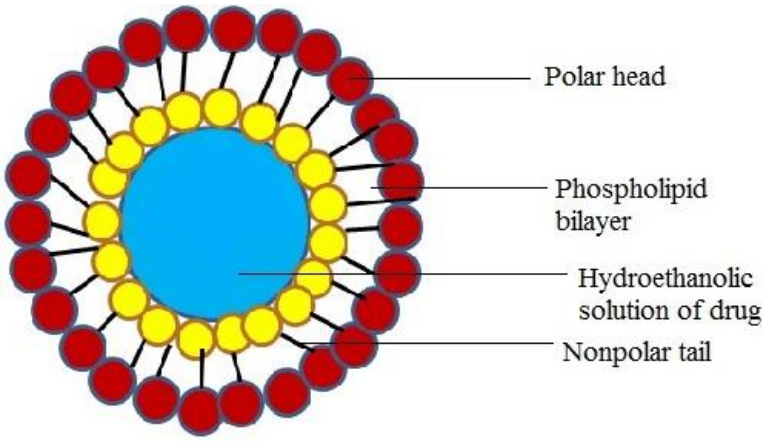

Fig 15 : - Ethosome

Table 9: Examples of Ethosomes used in the treatment of cancer:-

Polymer	Drug	Outcome	Reference
Hydroxypropyl- methacrylamide (HPMA)	Paclitaxel	Enhanced permeability and retention effect	56

Table 10: Cited patents of Ethosome in anticancer: -

Inventor	Current Assignee	Topic	Reference
Ramesh C. Pandey, Luben K. Yankov, Raghu Nair, Alex Pouley	Xechem International Inc	Preparation of brominated paclitaxel analogues and their use as effective antitumor agents	57

6. Dendrimers

Dendrimers are nanometer sized three dimensional branched structure macromolecules possess three distinctive layers core , branches and functional groups [58]. The effectiveness on targeting sites is achievedby attaching some targeting ligands at the external surface of dendrimers [59].

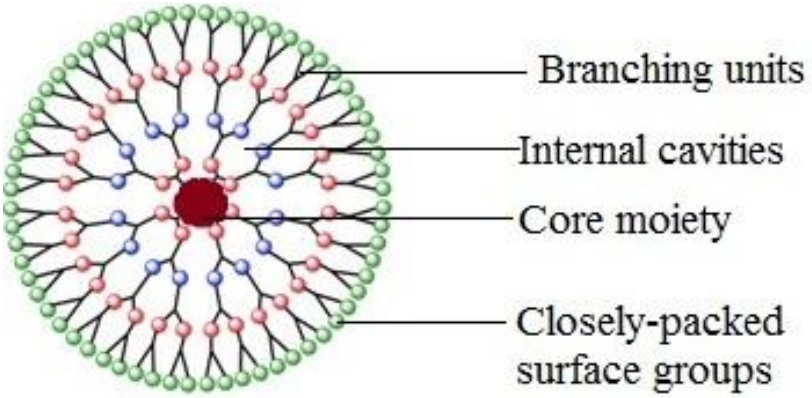

Fig 16 : - Dendrimer

Table 11: Examples of Dendrimers used in the treatment of cancer: -

Polymer	Drug	Outcome	Reference
PAMAM	Paclitaxel, doxorubicin	Improve the solubility	60

Table 12: Cited patents of Dendrimer in anticancer: -

Inventor	Current Assignee	Topic	Reference
Sang Van	Annam biosciences LLC	N-BOC- dendrimers and their conjugates	61

CONCLUSION: -

"As the review has reveals" it is clear that; In this article, i am: focusing on Novel drug delivery system, the novelty of existing drugs imparts huge benefits in cancer treatment. Novel drug delivery system is designed to improve the physiological condition of drug and the behaviour of active pharmaceutical ingredients. It is mainly used to improve the therapeutic effect of drug with its controlled release and targeted action. It eases the overall problems in cancer treatment along with therapies in respect to therapeutic effects, controlled release, physiological behaviour and site of action. Some examples of novel drug delivery system and their active drug which are used in the treatment of cancer like- microspheres active drug: – (doxorubicin), nanoparticles active drug: - (indomethacin)

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