

Review Article

A Review on Anticancer drug delivery through Micro based Structure

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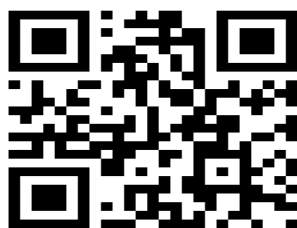
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ABSTRACT

The development of chemotherapy using conventional anticancer drugs has been hindered due to some drawbacks related to their poor water solubility and poor pharmacokinetics, leading to severe adverse side effects and multidrug resistance in patients. Micro carriers were developed to palliate these problems by improving drug delivery, opening the era of micro medicine in oncology. However, despite attractive results being obtained in preclinical studies, many well-designed micro drugs fell short of expectations when tested in patients, evidencing the gap between micro particle design and their clinical translation. The aim of this review is to evaluate the extent of micro therapeutics used in oncology. The reasons that prevent micro drugs from expanding to clinic are discussed, and the efforts that must be taken to take full advantage of the great potential of micro medicine are highlighted.

Keywords: Anticancer, microcarriers, drug delivery, oncology



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INTRODUCTION

Cancer is a disease characterized by uncontrolled multiplication and spread of abnormal forms of the body's own cells. The branch of medicine concerned with the study, diagnosis, treatment and prevention of cancer is Oncology. Cancer may affect people at all ages, even fetuses, but the risk of most varieties increase with age. [1] All cancers begin in cells, the body's basic unit of life. The body is made up of many types of cells. These cells grow and divide in a controlled way to produce more cells as they are required to keep the body healthy. When cell become old or damaged, they die and are replaced with new cells. However, sometimes this orderly process goes wrong. The genetic material [DNA] of a cell can become damaged, producing mutations that affect normal cell growth and division. When this happens, cells do not die when they should

and new cells form when the body does not need them. The extra cells may form a mass of tissue called a tumor. Targeted drug delivery is considered as a method in which drug-carrier complex, delivers drug to the pre-selected cell in a specific manner. The drug should reach the target cell[s] with the maximum concentration or with maximum effect. [2, 3] Cancer is an uncontrolled growth of cells resulting in lack of differentiation and ability to invade local tissues and metastasis which are reproduce individually throughout the body. During metastasis, cancer cells enter the blood stream and are carried to distant parts of the body where they form other similar growths. Synthetic drugs are available for the treatment of cancer but they are not free from unfavourable effects. Chemotherapy and radiation therapy are major clinical treatment used for the control

of early stages of tumor but these methods has severe side effects. [4]

Microparticles:

Microparticles are solid colloidal particles ranging from 10 to 1000 μm in size, they consist of micromolecular materials in which the active ingredients (drug or biologically active material) is dissolved, entrapped, encapsulated, adsorbed, or attached. [5] Microspheres have a monolithic-type structure [matrix] in which drugs are dispersed or adsorbed onto their surfaces or encapsulated within the particles. Microcapsules are the vesicular system in which the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. In this case the active substance is usually dissolved in the inner core, but may also be adsorbed to the capsule surface. [6,7] Apart from this, microparticles have some following advantages: Provide a targeted delivery of the drug, Protect drug from degradation, Decrease of toxic side effects, Improve the bioavailability of the drug, Cheaper and stable, Provide patient compliance. [8, 9]

Microtechnology:

Microtechnology is the preparation of Microsized structures containing the API. [10] Microtechnology is defined as the study and use of structures in the size range of 1 to 100 nm. The goal of microtechnology is to diagnose as accurately and early as possible and to treat as effectively as possible without any adverse effects using controlled and targeted drug delivery approach. [11] Important Drug Delivery System developed using Microtechnology principles are Microparticles, Solid Lipid Microparticles, Microsuspension, Microemulsion, Microcrystals. [12] Microparticles are the micronized particles, which transport pharmaceutical agents to achieve better or enhanced pharmacological effects. The use of microtechnology with combination chemotherapy provides synergistic in drug delivery.

Advantages of microparticle-based drug delivery therapy are:

- a) It enhances therapeutic effectiveness
- b) Reduces side effects of the drug payloads by improving their

pharmacokinetics properties

- c) Provides long circulation half lives
- d) Enhanced permeation and retention effect
- e) Drug safety
- f) Patient compliance

Aim and Objective:

This study is based on the overview on cancer, anticancer drugs and drug loaded microspheres. This review carried out to perform brief description about cancer, drugs that have anticancer activity and how to deliver in micro based system in treatment or/and chemoprevention of cancer.

Facts about Cancer:

- a) Cancers figure among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and 8.2 million cancer related deaths in 2012.
- b) The number of new cases is expected to rise by about 70% over the next 2 decades.
- c) Among men, the 5 most common sites of cancer diagnosed in 2012 were lung, prostate, stomach, and liver cancer.
- d) Among women the 5 most common sites diagnosed were, colon, rectum, lung, cervix, breast and stomach cancer.
- e) Cancer deaths are due to the 5 leading behavioural and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, alcohol use.
- f) Tobacco use is the most important risk factor for cancer causing around 20% of global cancer deaths and around 70% of global lung cancer deaths.
- g) Cancer causing viral infections such as HBV and HPV are responsible for up to 20% of cancer deaths in low-and middle-income countries
- h) More than 60% of world's total new annual cases occur in Africa, Asia and Central and South America. These regions account for 70% of the world's cancer deaths.

It is expected that annual cancer cases will

rise from 14 million in 2012 to 23 within the next two decades it will be 25 million.

Sl.	Type	Site of Cancer
1	Carcinomas	Cells that cover internal and external parts of the body such as lung, breast, and colon cancer.
2	Sarcoma	Bone, cartilage, fat, connective tissue, muscle and other supportive tissues.
3	Lymphomas	Lymph nodes and immune system tissues.
4	Leukaemias	Bone marrow and often accumulate in the bloodstream.
5	Adenomas	Thyroid, the pituitary gland, the adrenal gland and other glandular tissues.

Sign and Symptoms:

You should know some signs and symptoms of cancer. But remember, having any of these does not mean that you have cancer- many other things cause these sign and symptoms, too.

- Unexplained weight loss
- Fever
- Fatigue
- Pain
- Skin changes
- Change in bowel habits or bladder function
- Sores that do not heal
- White patches inside the mouth or white spots on the tongue
- Unusual bleeding or discharge
- Thickening or lump in the breast or other parts of the body
- Indigestion
- Recent change in a wart or mole or any new skin change
- Nagging cough
- Breathlessness
- Unexplained vaginal bleeding
- Persist heart burn or indigestion
- Croaky voice or hoarseness
- Looser poo or pooping more often
- Persistent bloating
- Difficulty swallowing
- Mouth or tongue ulcer that won't heal
- Heavy night sweats
- Unusual breast changes

Diagnosis:

If you have a symptom or your test result

suggests cancer, the doctor must find out whether it is due to cancer or some other cause. The doctor may ask about your personal and family medical history and do a physical exam. The doctor also may order lab tests, scans, or other tests or procedures.

Factors Influencing Cancer:

Age: Cancer most commonly develops in older people; 78% of all cancer diagnoses are in people 55 years of age or older. Anyone can develop cancer. However, the risk of being diagnosed with cancer increases significantly with age.

Obesity and Physical activity: Obesity and lack of physical activity are associated with increased risk at various cancer sites, including breast and endometrial cancer. [14]

Tobacco and Smoking: The consumption of tobacco is the leading cause of cancers. The regular use of tobacco via smoking, chewing, snuffing is responsible for 65% to 85% cancer incidences in men and women, respectively. [15]

Alcohol consumption: Alcohol consumption has been considered as one of the major causes of colorectal cancer as per a recent monograph of WHO. Annually, about 9.4% new colorectal cancer cases are attributed to the consumption of alcohol, globally. [15]

Radiation In the developed and developing countries, the radiations are also notorious carcinogens. About 10% cancer occurrence is due to radiation effect, both ionizing and non-ionizing. The major sources of radiations are radioactive compounds, ultraviolet [UV] and pulsed electromagnetic fields.

The mechanism on cancer therapy:

- Inhibiting cancer cell production directly by stimulating macrophage phagocytosis, enhancing natural killer cell activity.
- Promoting apoptosis of cancer cells by increasing production of interferon-I, interleukin2, immunoglobulin and complement in blood serum.
- Enforcing the necrosis of tumor and inhibiting its translocation and spread by blocking the blood source of tumor tissue.
- Enhancing the number of leukocytes and platelets by stimulating the haemopoietic function.
- Promoting the reverse transformation from tumor cells into normal cells.
- Promoting metabolism and preventing carcinogenesis of normal cells.
- Stimulating appetite, improving quality of sleep, relieving pain, thus benefiting patient's health. [16]

List of Some Anticancer Drugs:

The antineoplastic agents are not easily classified. Historically, they are categorized as (1) alkylating agents, (2) antimetabolites, (3) natural products, (4) hormones and antagonists, and (5) miscellaneous. In recent years, however, the miscellaneous group has come to include some of the most important agents.

- 1) Docetaxel
- 2) Paclitaxel
- 3) Anthracyclines
- 4) Doxorubicin
- 5) Epirubicin
- 6) Alkylating Agents
- 7) Cyclophosphamide
- 8) Vinca-Alkaloids
- 9) Vinorelbine [Intravenous]
- 10) Vinorelbine [Oral]
- 11) Anti-Metabolites
- 12) Fluorouracil
- 13) Capecitabine

Influence of Aging on Drug Pharmacokinetics:

With increasing age, multiple physiological parameters alter, which may substantially influence the PK of anticancer drugs. In

elderly patients, the PK profile can be influenced by changed distribution, metabolism and elimination parameters, while changes in absorption rarely led to clinically-relevant differences. Changes in gastric pH may have variable impacts on anticancer drug absorption, while absorption of Class II oral therapeutic drugs, including tyrosine kinase inhibitors and endocrine agents, increases with increasing gastric pH. [17,18] Another example includes capecitabine, with a higher absorption in elderly patients with a higher gastric pH, similar to increased absorption in the fed compared to the fasted state. These multifactorial and complex changes make it difficult to predict the net effect of aging on the PK profile of a specific drug administered to elderly breast cancer patients. Besides these physiological changes, multiple other factors contribute to the complexity of anticancer drug treatment in the elderly patient. Firstly, elderly patients often have several comorbidities and receive co-medication that may negatively affect anticancer treatment. For instance, patients with diabetes mellitus encountered more chemotherapy-related toxicities when receiving adjuvant chemotherapy for breast cancer compared to the non-diabetic control group. [19,20] A higher fat proportion in the elderly patient may result in impaired anticancer drug disposition and increased toxicity from various chemotherapy regimens. Furthermore, comorbidities were determined to significantly influence mortality rates in elderly patients diagnosed with cancer. [21,22]

CONCLUSION

After cardiovascular disease Cancer is the second leading cause of death. Cancer is the abnormal growth of cells in our bodies that can lead to death. Microsphere technology is the latest trend in cancer therapy. It helps the pharmacist to formulate the product with maximum therapeutic value and minimum or negligible range side effects. Cancer is a disease in which the abnormal cells are quite similar to the normal cells, with just minute genetic or functional change. A major

disadvantage of anticancer drugs is their lack of selectivity for tumor tissue alone, which causes severe side effects and results in low cure rates. Thus, it is very difficult to target abnormal cells by the conventional method of the drug delivery system. Microsphere technology is probably the only method that can be used for site-specific action, without causing significant side effects on normal cells.

REFERENCES

1. Roger Walker, Clive Edwards. Cancer disease. In Roger Walker, The Textbook of Clinical pharmacy and Therapeutics, Third Edition. New Delhi, Jaypee Brothers Medical Publishers [P] Ltd 2003; 265-353.
2. Peppas LB, Blanchette JO, Nanoparticle and targeted system for cancer therapy. *Adv Drug Deliv Rev.* 2004; 56: 1649-59.
3. Lee RJ, Low PS. Folate-mediated tumor cell targeting of liposome-entrapped doxorubicin in vitro. *Biochem Biophys Acta* 1995; 1233: 134-144.
4. S. Rajeshkumar, M. Nagalingam, M. Ponnankajamideen, M. Vanaja, C Malarkodi, "Anticancer 11. Sinha R, Anderson DE, McDonald SS, Greenwald P, "Cancer Risk and Diet in India" *J Postgrad Med.*, 2003; 49: 222-228.
5. Kreuter J, Nanoparticles-a historical perspective. *Int J Pharm.* 2007; 331: 1-10.
6. Mohanraj VJ, Chen Y. Nanoparticles – A Review. *Trop J Pharm Res.* 2006; 5 [1]: 561-73.
7. Soppimath KS, Aminabhavi TM, Kulkarni AR.; Biodegradable polymeric nanoparticles as drug delivery devices. *J Control Release* 2001; 70: 1–20.
8. Gelperina S, Kisich K, Heifets L. The Potential Advantages of Nanoparticle Drug Delivery Systems in Chemotherapy of Tuberculosis. *Am J Respir Crit Care Med.* 2005; 172[12]: 1487–1490.
9. Marcato PD, Duran N.; New Aspects of Nanopharmaceutical Delivery Systems. *J Nanosci Nanotechnol* 2008; 8[5]: 1-149.
10. Loxley A. et al. Solid Lipid Nanoparticles for the Delivery of Pharmaceutical Actives. *Drug Delivery Technology* 2009; 8-32.
11. Mishra B, et al. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. *Nanomedicine NMB* 2010; e9- e24.
12. Maravajhala V. et al. Nanotechnology in Development of Drug Delivery System. *International Journal of Pharmaceutical Science and Research* 2011; 3: 84-96.
13. Radha Sharma, Suman Jain, "Cancer Treatment: An Overview of Herbal Medicines" *WJPPS*, 2014; 3: 224.
14. Sinha R, Anderson DE, McDonald SS, Greenwald P, "Cancer Risk and Diet in India" *J Postgrad Med.*, 2003; 49: 222-228.
15. Imran Ali, Waseem A. Wani and Kishwar Saleem, "Cancer Scenario in India with Future Perspectives" *Cancer Therapy*, 2011; 8: 56-70.
16. Kharb Manju, Jat R.K. and Gupta Anju, "A Review on Medicinal Plants Used As A Source of Anticancer Agents" *International Journal of Drug Research and Technology*, 2012; 2[2]: 177-183.
17. Shah Alam, Pooja Satpathy, Aditi Thosar, "Plants And Its Parts As A Source Of Anti-Cancer Compounds: A Review" *IRJP*, 2014; 5[4]: 244-245.
18. Rajandeep Kaur, Jagpreet Singh, Gagandeep Singh, Harpreet Kaur, "Anticancer Plants: A Review" *J. Nat. Prod. Plant Resour.*, 2011; 1[4]: 131-136.
19. Srokowski, T.P.; Fang, S.; Hortobagyi, G.N.; Giordano, S.H. Impact of diabetes mellitus on complications and outcomes of adjuvant chemotherapy in older patients with breast cancer. *J. Clin. Oncol.* 2009, 27, 2170–2176. [CrossRef] [PubMed]
20. Satariano, W.A.; Ragland, D.R.; The effect of comorbidity on 3-year survival of women with primary breast cancer. *Ann. Intern. Med.* 1994, 120, 104–110. [CrossRef] [PubMed]
21. Yancik, R.; Wesley, M.N.; Ries, L.A.; Havlik, R.J.; Edwards, B.K.; Yates, J.W. Effect of age and comorbidity.
22. Shumaila A., Maryam S., Ayesha N.; A mini review on cancer and anticancer drugs; *IAJPS* 2016, 3 (11), 1383-1388.