Review on Anticancer Activity of Nanoparticles

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Purpose of anticancer activity of nanoparticles to increase the anticancer efficacy while reducing the side effects that are common in the treatment of cancer. Nanoparticles are of much importance while treating cancer because they are the nanoscale drug carriers. And this review will provides all the detail about the importance of nanaparticles in the treatment of cancer. Moreover this review also provides that how the nanoparticles target the tumor tissues and how they reach these tumor tissues or tumoral cells. This article will also elaborate that how these nanoparticles deliver the anticancer drug only to the tumor cells or tumoral tissues despite of the healty cells or healthy tissues. And this article also elaborate that how the nanoparticles cross the MDR resistance, which is due to the presence of P-glycoproteins system localized at the cancerous cell's membrane.

Abstract

Numerous investigations have shown that both tumoral cells and tumoral tissues can be controlled the entrapment of anticancer drug into the submicronic systems known as **nanoparticles**[1].The purpose of this sort of treatment is to increase the anticancer efficacy while reducing the side effects that are common in the treatment of cancer.Nanoparticles are of much importance while treating cancer because they are the nanoscale drug carriers.And this review will provides all the detail about the importance of nanaparticles in the treatment of cancer.Moreover this review also provides that how the nanoparticles target the tumor tissues and how they reach these tumor tissues or tumoral cells.This article will also elaborate that how these nanoparticles deliver the anticancer drug only to the tumor cells or tumoral tissues despite of the healty cells or healthy tissues.And this article also elaborate that how the nanoparticles cross the MDR resistance,which is due to the presence of P-glycoproteins system localized at the cancerous cell's membrane.Lastly this review also focuses on the safety issues related with the therapy of cancer by nanoparticles,that is due to their penetration ability to cells due to their extremely small size.

[1] [1] AD Maynard; RJ Aitken; T Butz; V Colvin; K Donaldson; G. Oberdörster; MA Philbert; J Ryan; A Seaton; V Stone; SS Tinkle; L Tran, NJ Walker; DB Warheit. Nature, 2006, 444, 267-269

Introduction:-

Cancer is defined as the uncontrolled division of cells that results in the formation of tumors and at that time cancer is the second leading cause of death globally and is responsible for an estimated 9.6 million deaths in 2018. Globally about 1 in 6 deaths is due to cancer.Approximately 70% deaths from cancer occurs in low or average income countries and it is because of its much expensive and inediquate treatment.And that's why it has became the most fatal disease in many countries .But there is a treatment for most types of cancers that is the targeting of tumor tissues or tumor cells with the nanoparticles and this targeting is of much importance in the treatment of cancer.If naoparticles are made properly and are delivered to the tumor tissues or tumor cells only then the cancerous cells can be killed and this can be done by the proper delivery and targeting of nanoparticles to the cancerous tissues or tumors.According to the process used for the synthesis of nanoparticles,two types of nanoparticles can be produced for the anticancer drug delivery that are **Nanocapsules**[2] and the **Nanospheres.**These two types of nanoparticles are on the basis of their anticancer drug carrying ability.Nanospheres are the matrix systems in which the anticancer drug is dispersed throughout the particles.While nanocapsules are the vesicular systems in which the anticancer drug is confined to an aqueous cavity surrounded by a single polymeric membrane.Hence the nanocapsules are considered as the reservoir systems for the treatment of cancer because of their safe drug delivery action. Nanoparticles and especially nanocapsules are used as a vehicle that have the ability to target tumor tissues or tumor cells because nanocapsules have the ability to protect the drug from premature inactivation of anticancer drug during its transport to tumor tissues or tumor cells .Moreover there are also some special types of nanoparticles available that are able to overcome the MDR resistance which is due to the presence of P-glycoprotein efflux system localized at the cancerous cell membrane .A controlled release of the drug content inside the tumoral interstitum may be achieved by controlling the nanoparticulate structure and the structure of nanoparticles may differ on the basis of polymer used and the way by which the drug is associated with the carrierthat are the adsorption or encapsulated.It means that we can control the anticancer activity of nanoparticles by controlling their structure .We can use these nanoparticles at cellular as well as tumor tissue level after some appropriate changes like

[2] [5] DA Tomalia; Aldrichimica Acta., 2004, 37(2), 39-57.

packing them in a DNA origami shell , after adding the genetic marker sequences that are added on both sides of the nanoparticles because these are recognized by cancerous cell or cancerous tissues.

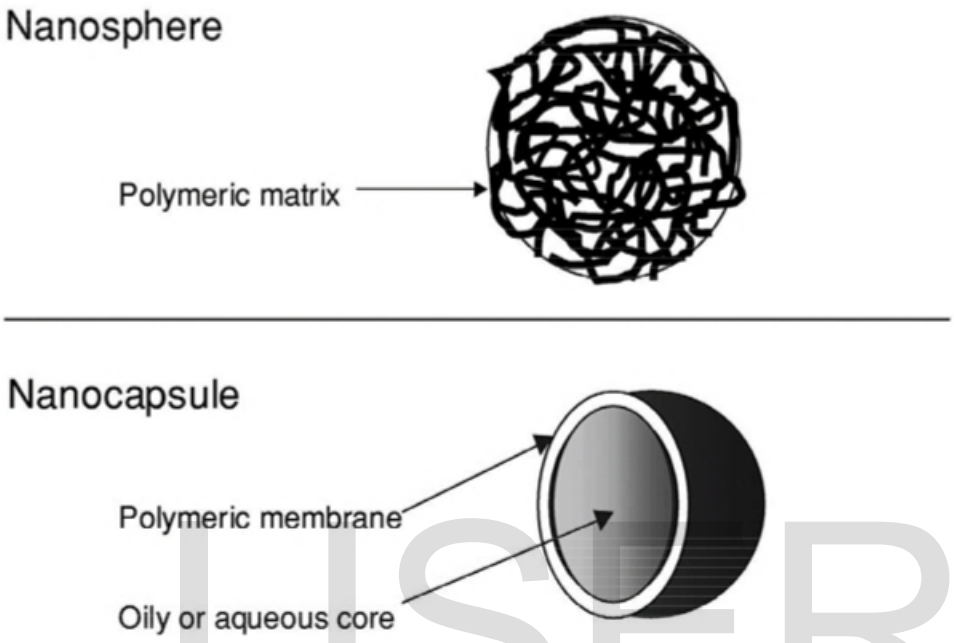

Fig. 1. Nanoparticles are: nanosphere (matrix systems) (top) or nanocapsule (reservoir system) (bottom).

Figure 1

1. Anticancer activity of nanoparticles :-

Nanoparticles are of much importance while treating with cancer due to their anticancer activity but this can only become if they are designed appropriately.Nanoparticles may act as a anticancer drug vehicles able to target tumor tissues or tumor cells , to a certain extent.And all the changes are done only to protect immature or premature inactivation of anticancer drug during its transport .A controlled release of the drug content inside the tumoral interstitum may be achieved by controlling the structure of nanoparticles.Firstly nanoparticles may differ on the basis of polymer used and secondly the way by which the drug is associated with the carrier that are the

adsorption[3] or the **encapsulation**[4].Moreover the most important changes that are done during the delivery and targeting of nanoparticles are the addition of marker sequences on both sides of the nanoparticles.And secondly the nanoparticles are packed in DNA origami shell for the proper shells for the proper delivery of nanoparticles to the tumoral tissues or the tumoral cells.Moreover, nanoparticles may also act at the cellular level.They can be **Endocytosed**[5] or **Phagocytosed**[6] by the cells,with a resulting cell incorporation of the encapsulated anticancer drug.

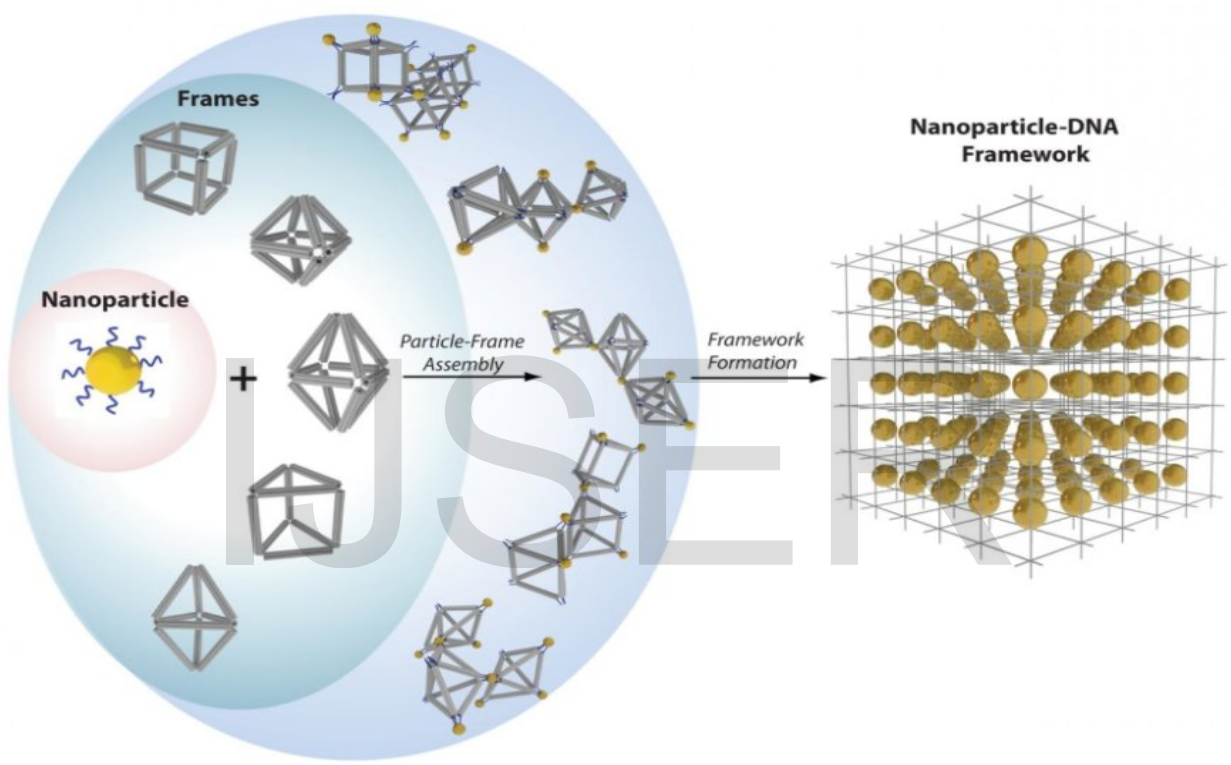

Figure 2

The greatest and the most immediate impact of nanotechnologies in cancer therapy is in the drug delivery.The therapeutic effect of nearly all drugs used in our daily life can be improved if they

[3] https://en.wikipedia.org/wiki/Adsorption
[4] https://en.wikipedia.org/wiki/Encapsulation_(computer_programming)
[5] https://en.wikipedia.org/wiki/Endocytosis
[6] https://en.wikipedia.org/wiki/Phagocytosis

are delivered more efficiently to their targets.A number of hurdles lying on the way of trating any disease may be overcome with various novel advancements of nano drug delivery.And the best way to increase the efficacy and reduce the toxicity of a cancer drug is to target this anticancer drug to the tumoral site.Moreover to maintain the concentration of anticancer drug at the tumoral site for a sufficient time for for its therapeutic action to take effect.Certain types of nanoparticles are also found that have the ability to overcome the MDR resisitance,which is due to the presence of P-glycoproteins efflux system localized at the cancerous cell membrane.Advantages of nanostructure-mediated drug delivery mainly include the ability of nanoparticles to deliver the anticancer drug directly into the cells.Moreover nano technology is the only treatment tool that has the ability or capacity to target the tumoral cells or tumors in the healthy tissue.Nano technology in the treatment of cancer has two main goals that are localized drug delivery and the specific targeting . And the newly produced nano devices (Nano pores,nano tubes,nano shells and the nanowires) has both the previously elaborated features and they can win laurels in the field of cancer .They have opened a new world of treating cancer.

2. Nanoparicles for tumor tissues targeting and delivery:-

Nanoparticles are used for targeting the tumor tissues.Basically the cancerous cell or cancerous tissues are quite different from the normal or healthy cells . A tumor marker is a substance found in the body tissues that can be elevated only in the cancerous cells and their rised level in any tissue is the representative of tumors at that place.These markers that are elevated in the tumoral cells are named as **oncomarkers**[7] and now in the nano technology modern nanoparticles are developed in which the various molecular markers are added that are complementary to the oncomarkers (present only in the tumoral cells or tumoral tissues).And these markers are basically the nucleotides sequences that are read by the oncomarker sequences and this is how the nanoparticles find the tumoral cells and tumoral tissues which is known as the targeting.The fist step (target the tumoral cells or tumoral tissues) is done through the addition of molecular sequences to the nanoparticles and now the second step in the treatment of cancer is the delivery

[7] https://en.wikipedia.org/wiki/Tumor_marker

of the anticancer drug(**Doxorubicin**[8]) that is present in the nanoparticles to the tumoral tissues or tumoral cells.

Nanoparticles has doxorubicin that is the most efficient anticancer drug.But doxorubicin can cause the death of the death of the normal cells too if it is released in a healthy tissue(that has some cancerous cells).So the direct delivery of Dox is harmful and we use the nanoscale capsules that have the ability to deliver the Dox only inside the cancerous cells.Nanoscale capsules recognize the cancerous cells by using oncomarkers as signatures.They also consisit up of DNA origami shells covered by immune factors with molecular binding sites on their surfaces.Nanoparticles are delivered in blood streams and then the DOX nanoparticles penetrate inside the cancer cells with the help of molecular sequences that are complementary to the oncomarker sequences present only in the cancerous cells.This is how nanaparticles recognize the cancerous cells and the cancerous cells are recognized.

Who will domain the school of thought of drug delivery?	
• NANOTECHNOLOGY	• MARKER SEQUENCING
Nanoparticles are extremely précised in targeting.	Marker sequencing is not achievable on clinical bases.

[8] https://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/cancer-drugs/drugs/doxorubicin

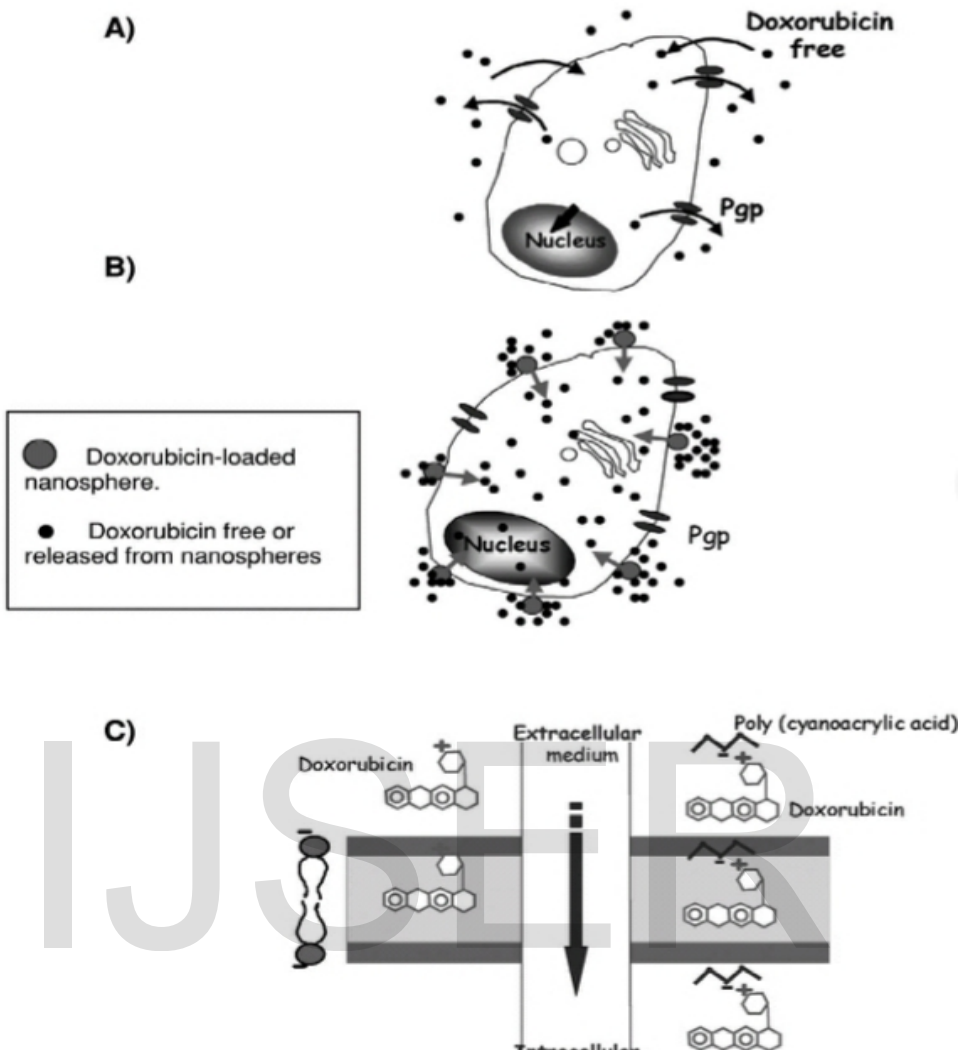

Figure 3

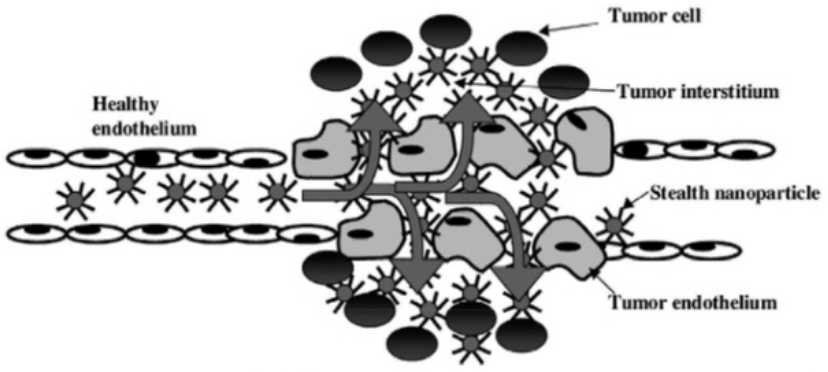

Fig. 2. Extravasation of long-circulating (Stealth™) nanoparticles in the tumor interstitium by passive diffusion or convection across the

Figure 4

When nanocapsules conjugated with several markers (complementary to the oncomarkers present only in the cancerous cells) reaches the targeted tumor tissues its marker sequences that are complementary to the oncomarker sequences are read by the cancerous cells and they (cancerous cells) allow these nanocapsules to enter.And then the DNA origami shell opens and start releasing DOX inside the cancerous cells.This is how the anticancer drug is successfully delivered (only in the cancerous cells) and the cancerous cells starts dieing due the direct delivery of DOX inside them.

1. Safety issues related with the use of nanoparticles:-

Despite the anticancer activity of nanoparticles,they have toxic effects too.And these toxic effects are due to their shapes and extremely small size .There is a fact that the shape and charge on nanoparticles that can accelerate the translocation through cell membranes up to 60 orders of magnitude.**Ag (Silver)** nanoparticles with varying shapes are reported to affect the cells in a diverse way.Keeping size and surface area same for one type of nanoparticles helps in evaluating their shape affecting toxicity.**ZnO (Zinc Oxide)** nanoparticles in shape of **nano-rods** [9]bring more toxicity for human lung's epithelium cells as compare to **spherical ZnO** nanoparticles.

As nanoparticles have extraordinary small sizes and due to extremely small size they have increased mobility,they can diffuse into animal or plant cells.Size of nanoparticles is inversely related to their diffusion capacity.Hence these nano-sized particles have comparatively higher and efficient penetrative potential in human and plant tissues than ordinary particles.Penetration level of nanoparticles across different barriers of cells are mostly size dependent.Decreased size exponentially increases surface area resulting in higher level of **oxidation** and **DNA damaging capabilities.**Nanoparticles with a **size of 35nm or less** are assumed to penetrate and cross the blood-brain barriers.And the particles with **size<40nm** or more have a potential to enter in the nuclei of cells and hence are extremely harmful.While those **with size upto 100nm** can cross or acess only cell membrane.

[9] https://en.wikipedia.org/wiki/Nanorod

Small size of nanoparticles is associated with increased nanosized penetrative potential which is then associated with higher toxicity by inducing **oxidative stress[10], genomic** and **mitochondrial DNA damage** and **apoptosis.**

[10] https://www.medicalnewstoday.com/articles/324863.php

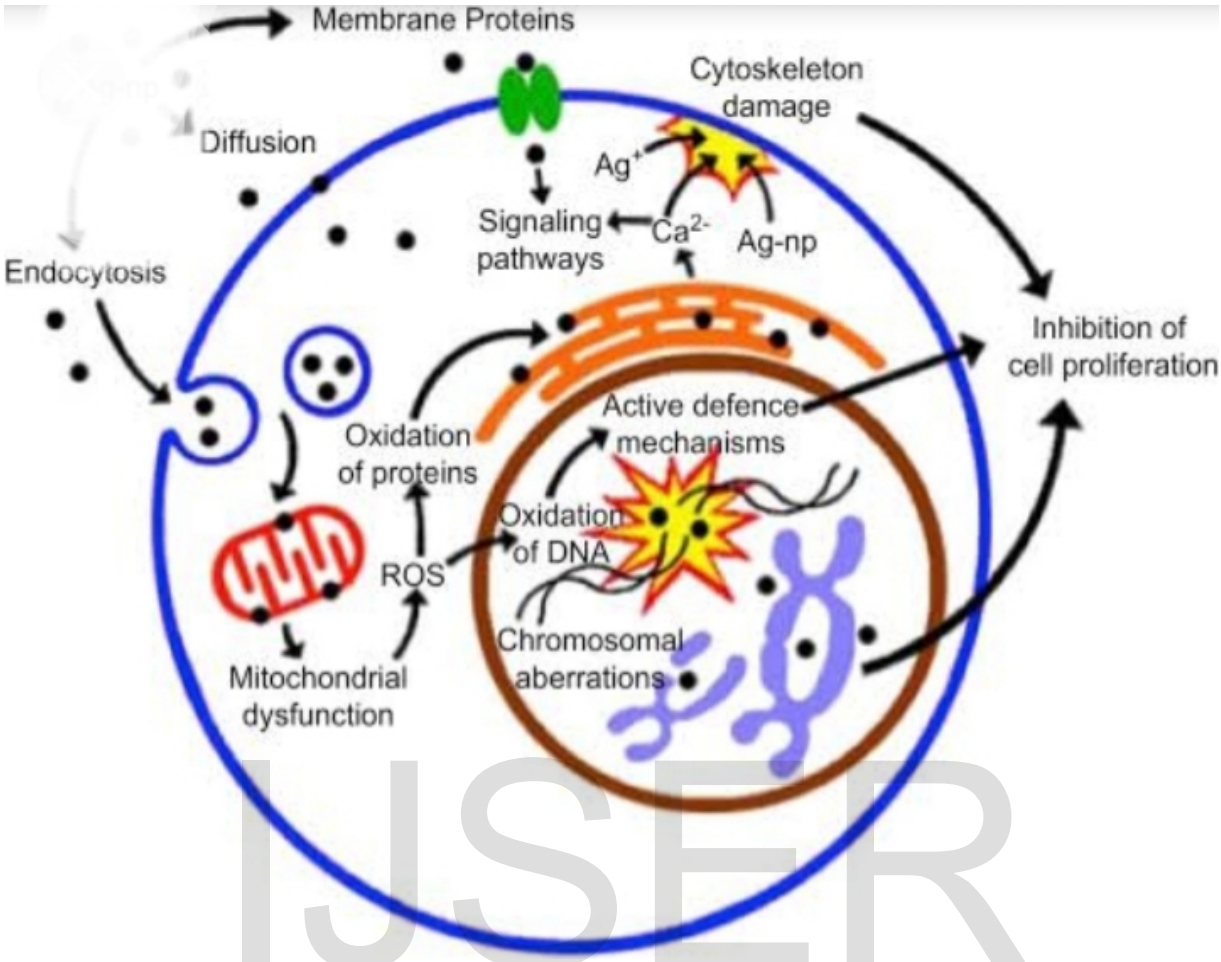

Figure 5

4-Conclusion

Despite the some harmful aspects (High penetration ability) nanoparticles are of much importance in the treatment of cancer because of their some extraordinary features that are their ability to cross the MDR resistance site present in the tumoral cells and tumoral tissues.Moreover, they also have the ability to recoznize the cancerous cells due to the molecular sequences (complementary to the oncomarker sequences) present on their memebranes and due to this extraordinary feature they will target only to the cancerous cells and not the healthy cells.This ability (targeting only cancerous cells) has done wonders in the field of cancer therapy.So lastly we can conclude that after some appropriate changes (described above) nanoparticles can be helpful in the theraupatic sense and we can not neglect their importance due due their some harms.

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