Content available at: https://www.ipinnovative.com/open-access-journals

International Journal of Pharmaceutical Chemistry and Analysis

Journal homepage: https://www.ijpca.org/

Editorial

Selectively targeting the cancer cells by reactivating the cell killing function of p53 protein

Chirag J. Gohil[1,*], Jigna J. Gohil[2]

[1]*Research Scholar, Discipline of Pharmacy, Gujarat Technological University, Ahmedabad, Gujarat, India*
[2]*General Practitioner Doctor, Gujarat, India*

ARTICLE INFO

Article history:
Received 02-07-2022
Accepted 20-07-2022
Available online 02-08-2022

Cancer is a major challenge for the medical science. It is one of the leading cause of the deaths in the many countries. There is a tumor formation occur in the cancer. And there are certain types of the tumors, like malignant tumor and benign tumor. Malignant tumor is more dangerous than benign tumor because it can spread from one part of the body to the other part. While benign tumor stay on one spot and demonstrate the limited growth. Cancer is characterized by the uncontrolled cell division and cell growth, which ultimately produce the tumor. There are many effective anti-cancer drugs are available in the market. But the main drawbacks of these drugs are that, they can't able to differentiate the cancer cells and normal cells. Hence, eventually they also kill the normal cell and produced the serious side effects like hair loss, gastric erosion, infertility and can damaged the vital organs.

For the normal growth and functioning of the body, cell division and cell growth is necessary. There is a specific type of controlling mechanism in our body which controls the cell division and cell growth, this process is called as "apoptosis". Apoptosis has been govern by various kind of proteins, among them principal protein if p53 protein. So this p53 protein is a tumor suppressor protein and prevents the cancer genesis. Approximately, in 50 % of the all kind of cancers, the function of this p53 protein has been inhibited, while rest of the cancers has found the way to bypass the p53 function. So we can say that inhibition of the p53 protein activity is responsible for the tumor/cancer occurrence. There are many reasons for the inhibition of the p53 protein function. But the main reason is its interaction with MDM2 protein. Actually MDM2 is a cancer genic protein.

MDM2 either bind with p53 protein or makes an inactive complex, or export out the p53 protein to outside cell. And at the lastly, directly induced the degradation of p53 protein. That is how MDM2 protein inactivates the p53 protein. So the cell killing process has been inhibited in the body. This protein-protein (p53-MDM2) interaction is the reason for the cancer.

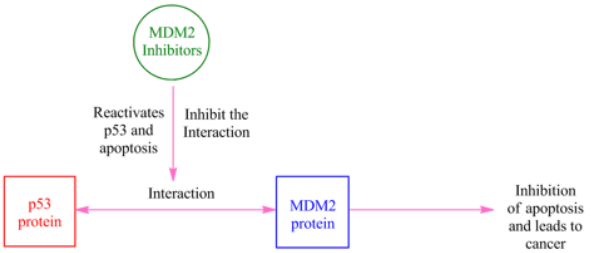
MDM2 so idea is that, if we can inhibit the p53-MDM2 interaction we can able to trigger the natural cell killing process of the body (apoptosis) in the cancer cells. Hence, we can selective target and kill the cancer cell only without producing the side effect to normal cells.

There are many strategies to inhibit this p53-MDM2 protein-protein interaction. We can inhibit this interaction by using natural molecules, by non-peptide small organic molecule or by peptide/protein molecules. The natural origin compounds to inhibit this interaction are very limited, because of less abundant of this kind of compounds in the nature. Mostly this type of natural p53 protein activator is from marine origin. While in the case of peptide/protein

* *Corresponding author*.
E-mail address: gohil2711@gmail.com (C. J. Gohil).

https://doi.org/10.18231/j.ijpca.2022.010

activators of p53 proteins also have some limitation and issue. Because of protein are very sensitive. So they got degraded by the digestive acid in the stomach (as like of egg and milk protein got degraded by heat and acids). And protein compounds may pose hypersensitivity and immune response in the patients. Along with these peptide or protein compounds have some technical difficulties too. Hence, among them Inhibition of the MDM2 protein activity by non-protein organic molecules (small molecules) is promising approach. If we design the non-protein organic molecule (small molecule) which can mimic the p53 protein so this small organic molecule will interact/bind with MDM2 protein and p53 protein will be free/spare. By this small organic molecule we can rescue the p53 protein and its function.



By this small organic molecule we can re-establish the p53 protein functions and its cancer cell killing mechanism. This will be very safe and effective approach for the cancer therapy.

The first small organic molecule (non-peptide) of this type was discovered in 2004, Its called “Nutlin”. Nutlin can reactivate the p53 function in cancer cells which contain un-mutated p53 prtein. According to clinical data, Nutlin and other small organic molecule (non-peptide) can induced the cell killing apoptosis in the cancer cells. While in the normal cells, it induced the dose dependent cell cycle arrest not the cell death. Hence, it is non-toxic to normal cells. But it cannot able to reactivate the apoptosis or p53 protein function in the cancer cell which contains the mutated p53 protein. So mutation of the p53 protein in the cancer cells makes them insensitive to this kind of treatment or compounds. This is the main limiting factor of this type of compounds. But we can overcome this limitation by investing the more scientific effort.

Since the discovery of Nutlin, many compounds of these types have been discovered and developed by the various Pharmaceutical companies and Universities. Among them, some of the compounds are under clinical trials. But currently there is no compound/drug of this class is available in the market.

We are working on the development of non-protein organic molecules (small molecule), which can inhibit the MDM2 protein function. So it prevents the p53-MDM2 protein-protein interaction. Hence we can restart the function of the p53 proteins in the cancer cells, which ultimately kills the cancer cells.

By this research work, we can selectively target the cancer cell only by our agents/compounds. So it will be nontoxic to normal cells. So it is smart approach to treat the cancer. And overall cancer patients will be benefitted by this. And it will be improve the public health and wellbeing of society and the nation.

Declaration

We confirm that this article has not been published elsewhere and is not under consideration by any of the journals. I have approved the article and agree with submission. The author has no conflicts of interest to declare.

Author biography

Chirag J. Gohil, Research Scholar

Jigna J. Gohil, General Practitioner

Cite this article: Gohil CJ, Gohil JJ. Selectively targeting the cancer cells by reactivating the cell killing function of p53 protein. *Int J Pharm Chem Anal* 2022;9(2):62-63.