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E-Mail :
editor.ijasem@gmail.com
editor@ijasem.org

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Analysis of the potential and anti-tumor effects of CAP in the treatment of cancer

DR. P. APARNA, B.GAYATRI, P. GAYARTRI DEVI

ABSTRACT: To be more precise, oral cancer is one of the leading causes of mortality in India and has a particularly negative impact on the country's northern and eastern regions. India accounts for nearly one-third of all oral cancer cases worldwide. A report based on 2018 data states that India has approximately 19999 new cases of mouth cancer and approximately 80 fatalities. We all understand quite well that the major components of all clinical methods to cancer treatment are chemotherapy, radiation therapy, and surgery. These therapies frequently result in morbid outcomes and lower the survival rate. They kill or hinder the growth of other cells due to the non-selective nature of cancer cells in comparison to normal cells. Recently, scientists and researchers have become quite interested in the potential of cold atmospheric plasma (CAP) in cancer treatment.

Cold Atmospheric Plasma (CAP), an ionised gas that is close to room temperature, has demonstrated its use in cancer therapy over the past ten years. Two CAP devices—the plasma jet and the dielectric barrier discharge—show remarkable anti-cancer activity against several hypodermic xenograft tumours in vivo treatment as well as millions of cancer cell lines in vitro. CAP is a targeted anti-cancer treatment method in contrast to standard anti-cancer strategies and medications. Therefore, there is still much work to be done in identifying the chemical and molecular basis of CAP's anti-cancer properties. This review is founded on a thorough introduction to the fundamentals of CAP, the current status of innovation competence in this area, the main difficulties, and future directions for cancer biologists.

Keywords: Cold plasma, cancer treatment, reactive species, selectivity

I. INTRODUCTION:

One of the leading causes of death in India is cancer. Despite being present around the world, oral cancer is more common in Southern and Orient Asia. About one-third of all cases worldwide originate in India. In 2018, the disease claimed 72,616 lives[1]. This is a really catastrophic amount to deal with, statistically speaking. Oral Squamous Cell Carcinoma (OSCC), the most common of all oral neoplasms, is frequently used in place of the phrase "oral cancer" in medical literature. According to reports, OSCC makes up over 90% of all oral neoplasms. The fourth state of matter is plasma[2]. Due to its ability to kill tumour cells selectively, non-thermal plasma (NTP) has grown significantly in favour in recent years in the field of cancer therapy employing cold plasma.

This is mostly because to the CAP's improved selective nature, which allows it to target and kill cancer cells with little to no collateral damage to healthy tissue. The effectiveness of CAP in eliminating ca[3,4]ncer cells is mostly attributed to reactive oxygen and nitrogen species (RONS). Although many attempts have been made to comprehend the fundamental workings of CAP in cancer treatment, thorough research with regard to various therapeutic scenarios is still lacking. More clinical trials should be encouraged to demonstrate the efficacy and relevance of the usage of CAP as a potential novel medicine in the near future.

Department of PHARMACEUTICS[1,2,3]
NRI College Of Pharmacy,
Pothavarappadu Village, Agiripalli Mandal, Krishna Dist,Andhra Pradesh Pin Code:521212

NTP/CAP: It is suggested that the Cold Atmospheric Plasma (CAP) technology be used in combination therapy to increase the effects of TMZ. By passing a large amount of alternating electric current through a gas, which causes a plasma glow discharge, CAP can be synthetically created in lab settings[5,6].

Actually, NTPs are an ionised gas mixture that also contains electrons, ions, neutral atoms, radicals, and UV photons. NTPs primarily function by activating the signalling pathway to induce apoptosis, preventing cell invasion and migration, or by stopping the cell cycle. The cancer cells are effectively treated with tools like plasma jets [7,8]. A plasma jet is made up of a wire electrode, a glass confinement tube with 8mm inner diameter and

10mm approx. outer dimeter, a Teflon fitting and a pen shaped nozzle having 2mminner diameter at the exit [9]. A sharp tipped tungsten pin wireis placed on the tube axis and the nozzle is attached to the glass tube end.

CAP and Oral Cancer:

Arecent study showed that the cancer type and culture conditions influences CAP treatment and hence need to be considered when selective activity of CAP is checked. These are considered as water channels that often facilitate the transport of free oxygen and nitrogen species, such as hydrogen peroxide as well as other small molecules including CO2, NO etc. Aquaporin 1.3 and 8 are known to play role in transport of H_2O_2 in mammalian cells. Studies show that over-expression of aquaporins to increases oxidative stress due to rising intracellular ROS concentration. Furthermore, monitoring the intracellular hydrogen peroxide content shows that the tumour cells accumulate H202 faster than the non-malignant ones CAPis composed of RONS, charged particles, LUV radiation and electromagnetic fields. All these synergistically act on the tumour cells[10,11].

But the main factor that contributes to cell death in oral cancer cells upon CAPtreatment is the ROS and RNS. In many studies primarily DSB have been assessed by detection of □H2AX, a phosphorylated form of the histone H2AX.Bishop et al. (2019) [12,13]

CAP in tumour microenvironment and Immunology:

The effects of CAP have been observed on different parts of the tumour microenvironment, which is majorly composed of malignant cells, immune cells, endothelial cells, fibroblasts tumour vasculature and the extracellular matrix, which are in constant communication with each other. In vitro studies have shown that CAP is able to destroy collagen. It is also reported that high doses of CAP prevent extracellular matrix interactions with cells and bone formation[14,15].

As the plasma treatment is a local therapy that possibly modulates the tumour microenvironment, various reports claim the possibility of plasma to stimulate immunity to support anticancer treatment [16,17]. Recently, two lines of research are going on in parallel to disentangle the effect of plasma treatment in anticancer immunity. One is the ability of plasma to affect immune cells directly, which leads to their activated ion or selection of specific subpopulations of immune cells, while the other is an indirect activation of immune cells via plasma- mediated tumour cell death and pro-inflammatory signals in the microenvironment [18,19].

CONCLUSION:

Reactive oxygen and nitrogen species (RONS) have been identified as the main contributors for the efficacy of CAP in killing oral cancer cells. However, many studies indicate a selective effect on CAP towards malignant cells compared to their healthy counterparts, the experimental settings in many of these studies may have influenced this finding. Furthermore, several factors have been 1dentified that often differ between healthy and malignant cells and hence, may contribute to an increased sensitivity of cancer cells to CAP. Factors such as expression of aquaporins, cholesterol or the ability to protect against oxidative stress by the anti-0xidative system determine how many RONS can enter the cell and interfere with intracellular signalling pathways. CAP treatment often results in reduced adhesion, migration and invasion and may contribute to a successful cancer treatment by reducing the ability of the cells to spread and form metastasis.

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