Are cigarette substitutes a safe alternative? It depends on user habits

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Cigarette smoking kills approximately 440,000 Americans each year, according to the Centers for Disease Control and Protection. It's the leading cause of preventable death worldwide. In order to overcome this addiction, many people resort to nicotine replacement therapies.

A recent literature review study by researchers at the University of Miami (UM) suggest that small dosages of nicotine found in cigarette substitutes could be harmful to human musculoskeletal system, due to overuse. The findings are reported in the *Global Journal of Medical Research*.

The researchers investigated and summarized the last five years of studies, on the effect of nicotine on wound and skeletal healing processes in humans, via PubMed database.

The report suggest that more information is needed on the potential effect of cigarette substitutes like Electronic cigarettes (E-cigarettes), which are fairly new to the market and not regulated by the Food and Drug Administration (FDA).

"E-cigarettes are marketed as safe alternatives to cigarette smoking, however the harms associated with their overuse have not yet been widely investigated," said Herman S. Cheung, James L. Night Professor in the UM College of Engineering, and senior author of the report. "We hope to increase awareness and promote further investigations into this field."

Interestingly, the findings show that nicotine can be beneficial at low dosages. For example, exposure to low dosages of nicotine promotes collagen production and skin wound repair. Yet at higher dosages cells involved in the wound and skeletal healing processes actually become ineffective. That's why overuse of nicotine-replacement, which still contain small amounts of nicotine, can present a health risk. However, what constitutes a low or high dosage depends on the cell type.

"Not all cells respond to nicotine in the same manner. What could be a low dosage for one is a high dosage for another," said Carlos M. Carballosa, doctoral student in the Department of Biomedical Engineering at the UM College of Engineering and primary author of this review. "The effects are to some extent, reversible, once exposure to nicotine stops."

The consequences of nicotine overuse are not necessarily new findings. However; the specific effects of nicotine on stem cells and the musculoskeletal system are. Stem cells are generic cells that can give rise to specific cell types in the body, through a process called cell differentiation. These cells play a crucial role in tissue regeneration and healing. Any changes to their natural function can significantly alter these processes.

"It has been widely documented that smokers, compared to non-smokers, experience prolonged delays in bone healing, after a bone fracture," Cheung said. "There are many theories as to why. "We believe that nicotine significantly affects the potential for stem cell proliferation, migration and osteogenic differentiation- the potential of a cell to become a bone cell," he said. "We think that these effects cause delays to bone healing."

The mechanisms behind the effects of nicotine on the musculoskeletal health are not fully understood. However, studies show that proteins called nicotine acetylcholine receptors (nAChRS) sit on the surface of the cells in the musculoskeletal system and act as mediators of the effects of nicotine on the cells.

There is a molecule called micro ribonucleic acid (miRNA), which is found throughout the body. miRNAs are instrumental in regulating the process that allows a stem cell to differentiate into a specific

type of cell, like a muscle, or a bone cell. The researchers believe that when nAChRS are exposed to nicotine, they affect the expression of miRNAs. However, it is not yet known if this is truly the case.

"The effect of nicotine on miRNAs is the focus of our current research," Carballosa said. "However, the link between nicotine exposure and expression of miRNAs implies that there is a correlation between the two."

More information: The study is titled "Nicotine's influence on musculoskeletal healing: A review featuring nAChRS and miRNA"

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