ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)
IJDSIR : Dental Publication Service
Available Online at: www.ijdsir.com
Volume – 6, Issue – 2, April - 2023, Page No. : 123 – 131

A narrative review on plasma therapy- when cosmos meets dentistry.

[1]Dr. Moitri Ojha, Assistant Professor, Department of Periodontology, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, Uttar Pradesh, India.

[2]Dr. Nimish Agarwal, Reader, Department of Oral and Maxillofacial surgery, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, Uttar Pradesh, India.

[3]Dr. Haritma Nigam, Associate Professor, Department of Oral Medicine and Radiology, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, Uttar Pradesh, India.

[4]Dr. Shekhar Prasad, Assistant Professor, Department of Prosthodontics, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, Uttar Pradesh, India.

Corresponding Author: Dr. Moitri Ojha, Assistant Professor, Department of Periodontology, TMU Dental College and Research Centre, Moradabad, Uttar Pradesh, India.

Citation of This Article: Dr. Moitri Ojha, Dr. Nimish Agarwal, Dr. Haritma Nigam, Dr. Shekhar Prasad, "A Narrative Review on Plasma Therapy- When Cosmos Meets Dentistry", IJDSIR - April - 2023, Volume – 6, Issue - 2, P. No. 123 – 131.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

The universe hides mysteries yet to be resolved. Over the time, geophysicists have analyzed the extreme events occurring in the universe and studied the behavior of fundamental constituents. Some of them have proven to be useful for application in commercial industries, transport and in medical practices. One such element is plasma which has been extensively studied in medical and dental therapeutics. It is an inherently powerful technology that interplays with redox biology. The application of plasma in dentistry displayed numerous unique advantages over conventional approaches. Hence, this review elucidates the current and future prospects of the application of plasma therapy in dentistry.

Keywords: Plasma, sterilization, redox biology, bactericidal.

Introduction

Plasma, the fourth state of matter that lays the fundamentals of cosmology, is the most widely researched topic in thermal science and astrophysics today. The term "plasma" was first coined byIrving Langmuir who received the Nobel Prize for chemistry in the year 1932.[1] Around 99.99% of the visible universe is composed of plasma- the sun, stars, nebulae, neutron stars, solar winds, black holes and the magnetosphere of the earth. Also, it forms the interplanetary, intergalactic and interstellar medium.

[2]Plasma can be synthesized artificially in laboratories by the application of electric, light and magnetic field across a gas where electrons are pulled away from its parent atom. At the atomic and subatomic levels, events like inelastic collision, radiation interactions and electron impact and exchange occur. This yields a superheated state of ionized matter saturated with electrically active and charged particles.[1]Unlike in space, plasma does not exist naturally on earth's surface. Researchers have successfully generated two forms of artificial plasma- Hot and Cold. The hot/thermal plasma is electrically produced at a high pressure whereas the cold/non-thermal plasma is generated at low temperature and pressure.[1]

Artificial plasma has found its application in various industries like- microelectronics, packaging industries, food industries, petrochemical industries, etc.[3]Currently, the use of plasma is overwhelming the medical science. It took 25 years of laborious work from its initial discovery to its fundamental application in therapeutic research.[4]The pioneer/initial experiments conducted in bioscience focused on bacterial cells destruction and sterilization. Slowly, the use of plasma has encroached on several arenas of oncology, wound healing, regeneration etc.[5,6]

In dentistry, plasma therapy is being recognized as a novel, advanced and innovative multipurpose technology. However, the research is still in its infancy and requires modification of the existing ideas and integration of concepts from several interdisciplinary experts. Hence this review delves deep into the possible applications and the future aspects of plasma in dentistry.

Mode of action

The biological activity of plasma is due to the highly energetic, free and extremely mobile electrons that can transfer electrical charges to cells and tissues. The most frequently employed plasma in bioscience is the non-thermal dielectric barrier discharged (DBD) plasma. This jet/tube exhibits a safe temperature range (below 40 degrees Celsius) that does not injure cells or biological tissues.[7]There are two modes of application on tissues- direct and indirect.

Direct method

The direct method involves plasma exposure to the biological target. This application is used in sterilization to inactivate bacteria and destruction of biofilms on wounds, medical equipment's, food and agricultural products. Also, the selective application of direct exposure can destroy cancer cells. Today, the hub of plasma medicine concentrates on the possibility to extend direct contact of plasma therapy with the biological setting.

Indirect Method

In indirect exposure, a liquid medium (water or culture medium) is first activated by plasma and then the same is applied on tissue

Plasma In Medicine[8,9]

It was soon realized that plasma possesses properties that can be exploited to open up new horizons in biomedical application. It is hypothesized that plasma interplays with redox biology; i.e. it introduces reactive and excited radical species in the tissue environment. These species include hydrogen peroxide, H_2O_2, nitrite, NO−2NO2-, nitrate, NO−3NO3-, peroxynitrite, $ONOO^-$, and organic radicals. Intensive works were carried out to comprehend the cellular response to plasma therapy which includes. :

- Cellular proliferation and angiogenesis which promotes wound closure and re-epithelization. Hence, causes effective wound healing.

- An innovative approach for sterilization and disinfection
- Improves cell permeabilization
- Facilitates effective coagulation which is more rapid than the natural process of coagulation.
- Selective killing of cancer cells by programmed cell death, otherwise known as apoptosis
- Cosmetic rejuvenation of face -as an "anti-wrinkle" agent

More recently,

- Acidification of lipid film surfaces by non-thermal DB Dat atmospheric pressure in the air.
- Degradation of adhesion molecules of G 361melanoma cells
- Reduction and degradation of amyloid masses by a pulsed radio-frequency.

Plasma in dentistry

Sterilization

Sterilization ensures high-quality patient service and forms the pillar in healthcare sector. The most frequently used method used is steam sterilization. Its drawback lies in the fact that it is unable to sterilize heat sensitive instruments. Plasma gas sterilization was first introduced in the year 1972 and has been considered a substitute to steam sterilization. This method of sterilization was approved by FDA in 1991.[10] It is a well-known fact that plasma can damage microbial cell structure via the physic-chemical method and is classified as a broad-spectrum antimicrobial agent. The underlying mechanism is that it serves as a rich source of active species (ions, electrons, radicals, UV light, vacuum UV (VUV), electric fields and metastable) depending on the gas used. The above-mentioned species can leach the bacterial membrane and can cause DNA strand breakage. A phenomenon- "intrinsic desorption" follows in the microbial cell structure where the chemical bonds are destroyed leading to the formation of volatile organic compounds.[11] By far, oxygen is the most common and frequently used gas that produces free oxygen radicals. A few authors have also recommended the use of nitrogen and other noble gases like helium, neon, argon and xenon. It is believed that plasma can deactivate spores, prions and endotoxins.[12]In this COVID era, the use of plasma as a source of disinfection has been appreciated.

Biofilm deactivation

Dental plaque is an aggregation of micro-organisms encased in a matrix of organic and inorganic components. It is said to be the culprit for periodontitis and dental caries that present features like- enhanced virulence and antibiotic resistance.[13] Mechanical and chemical modalities to eliminate plaque are implemented by professional and personal means. However, it is practically impossible to eradicate pathogens from all sites by mechanical methods. Chemical plaque control can demonstrate certain drawbacks like mucosal dryness and irritation, staining of teeth, altered taste sensation, etc. Hence, constant efforts to develop new strategies to deactivate this plaque biofilm is made by researchers and periodontists.[14] It has been clarified that plasma generates a plethora of reactive unstable ions eager to react with a substrate. These ions destroy pathogens and are effective in assassinating the bacterial population to a nearly undetectable level thereby achieving 100% bactericidal effect.[15]Ziuzina et al. evaluated the response of quorum sensing and virulence of P. aeruginosa, E. coli and L.monocytogens to cold plasma and concluded that the therapy is a potential approach to inactivate bacterial events.[16] Qing Hong et al. conducted a trial to demonstrate the effect of atmospheric plasma therapy on S.mutans species. The results suggested that not only plasma helped in reducing the bacterial count, but also

increased the susceptibility of bacteria to antibiotics and host immunity.[17] Hong Q et. assessed the efficacy of plasma against P.gingivalis bacteria- a periodontopathogen, by employing several assays like MTT, CFU, biofilm recovery and antibiotic susceptibility. It was concluded that not only plasma enables bacterial killing but also inhibits antibiotic resistance and repopulation of bacterial colonies.[18]

Implant surface modification

The quality, design and features incorporated in implants during their manufacture determine their success rate. At the molecular level, a cascade of events follows when implant surface communicates with the oral biofluids and bone.[19]Attempts have been made consistently to optimize the performance of implant for better Osseo integration by modifying the implant surface yet maintaining its desirable properties. One such method involves coating the implant surface with thermally melted materials using plasma.[20]

This method of treatment adopts the idea of homogenous deposition of titanium particles by injecting its powder form into a plasma torch which is then propelled against the surface at a high velocity. A layer of 40-50 μm thickness of titanium is deposited with an average roughness of 7μm. The roughness produced aids to increase the surface area and tensile strength at the bone-implant interface.[21]A rougher surface also shortens the healing period. Plasma-treated implants have the advantage of altered surface wettability due to less carbon content which modulates cellular response and adhesion. Also, plasma operating at the chair side has been introduced with the idea of implant exposure before the therapy which has demonstrated reduced contact angle. This aids in enhanced activities of osteoblasts.[22]

Plasma-sprayed hydroxyapatite coatings on implant surface are acknowledged by many manufacturers due to the rapid, well-controlled and homogenous deposition. In the process, various byproducts like tricalcium phosphate, tetra calcium phosphate and amorphous calcium phosphate are formed that permit the formation of apatite crystals during osseointegration. However, few authors have anticipated that plasma treatments can result in alterations in the metallic microstructure of implant surfaces.[23,24]

Plasma-treated zirconia implants are receiving more attention than traditional titanium implants due to their exclusive esthetic qualities. Enhanced hydrophilicityis another property of plasma-treated implants which have been proven in in vitro and in vivo studies.

Dental caries

Argon plasma toothbrushes have been recognized to reduce the microbial population responsible for dental caries (L. acidophilus and S. mutans).[25] Yang et al. suggested that decontamination is achieved within 15seconds for S. mutans and within 5 minutes for L.acidophilus species.[26]Qiao et al., in their in vitro experiment subjected a cultured biofilm model of S. mutans to plasma-activated water (PAW)for ten minutes. The authors witnessed the efficiency of PAW as a potential germicidal agent.

Studies have also advocated that cold plasma (Helium, Argon and DBD) can induce modifications in the hydroxyapatite crystals of enamel. This includes alterations in the hydrophilic and hydrophobic nature, the charge distribution, surface adsorption capacity and alterations in the chemical bonds. Recently, it has been proposed that plasma can enhance fluoride uptake which imparts antibacterial properties and can strengthen the enamel framework.[27]

Active plasma can reach inaccessible areas, crevices, grooves and small spaces. Eva Stoffel did groundbreaking research on the use of plasma needles in

dental caries as a disinfectant. This system enjoys the advantage of drill-free technology, hence can be used in anxious and apprehensive patients.[28] It is a minimally conservative approach which does not cause bulk removal of the tooth structure.

Traditional root canal therapies cannot eliminate pathogens completely and can re-populate the canals causing relapse. A continuous quest for an ideal disinfectant with optimum anti-pathogenic action and least side effects is in progress. Owing to the bactericidal nature of cold plasma, several investigations have been carried out to scrutinize its success in root canal treatments. Plasma can destroy the lipopolysaccharide layer of gram-negative bacteria causing cell leakage besides triggering degradation of bacterial DNA.[29]Ameneh et al compared the antibacterial outcome of plasma with photodynamic therapy (PDT) in root canals infected with Enterococcus faecalis (a bacteria responsible for failures in endodontic treatment). They concluded that the plasma therapy was efficacious in killing the population of these bacteria.[30]Jie Pan et al. performed an in vitro trial to study the performance of plasma in reducing the strains of E. fecalis. The study displayed the effective biocidal property of plasma against these organisms.[29]

Tooth bleaching

The removal of intrinsic stains by clinicians has always been a mammoth task. Conventional tooth bleaching employs a light source which have been said to abuse pulp via thermal damage. Plasma generates reactive species that professionally remove the surface proteins adsorbed on the tooth surface accountable for staining.[31] Lee et al., in their study removed surface stains from extracted teeth using plasma, thereby proving its potency as a whitening agent. The same authors conducted further studies and suggested that plasma jets can be used in association with hydrogen peroxide, thus causing a synergistic effect. A gas-liquid hybrid plasma system was developed via radiofrequency and the same was used by Kim et al as a novel method to successfully bleach teeth.[32]Seoul et al, on the other hand used 15% carbamide with plasma for whitening of teeth.[33]Burak et al. in their in vitro study confirmed that deionized water with NTAPP can substitute common bleaching agents.[34]

Adhesive restoration

Glow discharge polymerization, also called plasma polymerization utilizes the concept of monomer activation to initiate polymerization and aims to replace wet-chemical process. The marvel was witnessed by Sir Wilde and Thernard who observed the formation of high molecular weight solid products in a plasma of organic vapors. Later many researches about the deposition of organic and metallo-organic coating on substrates were performed.[35]A polymer surface when exposed to plasma creates free radical species and activates the surface. It is then exposed to air which allows grafting of monomers. The surface topography, hardness, elastic module, energy and roughness is modified at the micro and Nano-scale which overall results in better cross-linking of polymers and imparts wear resistance to the substance.

Plasma arc is gaining popularity for polymerization of composite restorations since it consumes shorter curing time. Studies have demonstrated that plasma treatment have also contributed differently to the penetration of individual components of the model adhesive due to their distinct hydrophilicity.

Oral diseases

Yixin et al. compared the efficacy of plasma with phase-I therapy for the treatment of ligature- induced periodontitis in rats. The study presented that cold plasma plays a role in modulating the host-mediated

inflammatory and immune response by reducing the expression of osteoclasts, RANKL and pro-inflammatory cytokines.[36]NTP can be used as a line of treatment in oral squamous cell carcinoma. Plasma irradiated medium has been used to destroy glioblastoma, ovarian, and gastric cancer cells. Cancer cells are oxidatively stressed. They bear a higher number of aquaporins and are prone to lipid peroxidation thereby facilitating entry of reactive species inside the cell. It is hypothesized that NTP can selectively kill these cells by ferroptosis process. The therapeutic technique can hinder the migration and invasion of cancer cells by reducing the expression of integrins. Since oral cavity directly communicates with the external environment, application of this therapy will be more accessible by the clinicians.[37,38]Candida albicans has been associated with root caries, early carious lesions in children and oral Candidiasis. The activity of plasma against this fungus was appreciated in the study conducted by Laurita et al., where deionized water (DIW), phosphate buffer (PB) and electrolyte solution (ES) from sodium dihydrogen phosphate in DIW, were treated by air DBD plasma.[39] Another study by Neda et al. proved the efficacy of NTP as an antifungal agent where strains of C. albicans was irradiated with plasma at 90, 120, 150 and 180seconds. The study illustrated that NTP inhibits the ergosterol synthesis in fungus besides hindering the activities of phosphoplipase and proteinase.[40]

Anti-inflammatory and antisepsis

The significance of plasma therapy has been highlighted in wound healing and antisepsis. The primary effect of plasma on a wound is disinfection and has been considered as an alternative therapy in patients with multidrug resistant therapy.[41]Few studies have suggested that plasma can cause multiple effects in mammalian cells which include interaction with subcellular components like DNA, proteins and human keratinocytes. Plasma can promote wound debridement in a single step by deactivating endotoxins and eliminating tissue- degrading enzymes (proteinase, hyaluronidase). At the molecular level, the low level of ROS produced in the process can encourage angiogenesis and promote intracellular signalling. Also, the state of the wound is transformed from a chronic stagnant stage to an active healing phase.[42]

Conclusion

The physiochemical nature of plasma is complex and depends on factors like temperature, pressure, environment, electrode configuration, source geometry and the composition of the gaseous mixture selected. The technology collaborates ideas from various fields like physics, chemistry, biotechnology and medicine. It is a promising, new and technically advanced scheme that serves multiple disciplines in dentistry. Further understanding and theoretical clarifications of cellular and molecular events in a biological tissue occurring in the presence of plasma is required whichwould help to resolve many mysteries.

References

1. Wilson H. The impact of plasma physics on the timescale to a tokamak fusion power plant. Philo's Trans A Math PhysEng Sci. 2019;377(2141):20170435.
2. Goertz CK. Plasma physics. Science. 1982;217(4566):1243-1244.
3. Fujisawa A. Review of plasma turbulence experiments. ProcJpnAcadSer B PhysBiol Sci. 2021;97(3):103-119.
4. Choi EH, Uhm HS, Kaushik NK. Plasma bioscience and its application to medicine. AAPPS Bulletin. 2021;31(1):10.

5. Bekeschus S, Schmidt A, Niessner F, Gerling T, Weltmann KD, Wende K. Basic Research in Plasma Medicine - A Throughput Approach from Liquids to Cells. J Vis Exp. 2017;(129):56331.
6. Graves DB. The emerging role of reactive oxygen and nitrogen species in redox biology and some implications for plasma applications to medicine and biology. Journal of Physics D-Applied Physics. 2012;45(26):263001
7. Lomaev MI, Sosnin EA, Tarasenko VF, Shitts DV, Skakun VS, Erofeev MV: Capacitive and barrier discharge excilamps and their applications. InstrumExp Tech. 2006, 49: 595-746.
8. Weltmann KD, et al. Atmospheric-pressure plasma sources: Prospective tools for plasma medicine. Pure Appl Chem. 2010;82(6):1223–1237.
9. Laroussi, M. Plasma Medicine: A Brief Introduction. Plasma **2018**; 1: 47-60.
10. Shintani H, Sakudo A, Burke P, McDonnell G. Gas plasma sterilization of microorganisms and mechanisms of action. ExpTher Med. 2010;1(5):731-738.
11. Shintani H, Shimizu N, Imanishi Y, Sekiya T, Tamazawa K, Taniguchi A, Kido N. Inactivation of microorganisms and endotoxins by low temperature nitrogen gas plasma exposure. Biocontrol Sci. 2007;12:131–143.
12. Kim S-M, Kim J-I. Decomposition of biological macromolecules by plasma generated with helium and oxygen. J Microbiol. 2006;44:466–471.
13. Marsh PD. Dental plaque as a biofilm and a microbial community - implications for health and disease. BMC Oral Health. 2006;6 (1): 1-14.
14. Vyas T, Bhatt G, Gaur A, Sharma C, Sharma A, Nagi R. Chemical plaque control - A brief review. J Family Med Prim Care. 2021;10(4):1562-1568.
15. Ranjan R, Krishnamraju PV, Shankar T, Gowd S. Nonthermal Plasma in Dentistry: An Update. J IntSocPrev Community Dent. 2017;7(3):71-75.
16. Ziuzina D, Boehm D, Patil S, Cullen PJ, Bourke P. Cold Plasma Inactivation of Bacterial Biofilms and Reduction of Quorum Sensing Regulated Virulence Factors. PLoS One. 2015;10(9):0138209.
17. Hong Q, Dong X, Chen M, et al. An in vitro and in vivo study of plasma treatment effects on oral biofilms. J Oral Microbiol. 2019;11(1):1603524
18. Hong Q, Sun H, Chen M, Zhang S, Yu Q. Plasma treatment effects on destruction and recovery of Porphyromonasgingivalis biofilms. PLoS One. 2022;17(9): 0274523.
19. Yeo IL. Modifications of Dental Implant Surfaces at the Micro- and Nano-Level for Enhanced Osseointegration. Materials (Basel). 2019;13(1):89.
20. Dr.Sreeharsha TV, Dr.SmithaSharan, Dr.Brunda K, Dr. Pradeep Chandra K, Dr.ItiBadola and Dr.NadiraJabeen S. Implant surface modifications: A review. International Journal of Applied Dental Sciences 2020; 6(3): 334-338
21. Tsujita H, Nishizaki H, Miyake A, Takao S, Komasa S. Effect of Plasma Treatment on Titanium Surface on the Tissue Surrounding Implant Material. Int J Mol Sci. 2021;22(13):6931.
22. Vercaigne S, Wolke JG, Naert I, Jansen JA. Bone healing capacity of titanium plasma-sprayed and hydroxylapatite-coated oral implants. Clin Oral Implants Res. 1998;9(4):261-271.
23. Talib RJ, Toff MR. Plasma-sprayed coating of hydroxyapatite on metal implants--a review. Med J Malaysia. 2004;59Suppl B:153-154.
24. MacDonald DE, Betts F, Stranick M, Doty S, Boskey AL. Physicochemical study of plasma-

sprayed hydroxyapatite-coated implants in humans. J Biomed Mater Res. 2001;54(4):480-490.

25. Ritts AC, Li H, Yu Q, et al. Dentin surface treatment using a non-thermal argon plasma brush for interfacial bonding improvement in composite restoration. Eur J Oral Sci. 2010;118(5):510-516.
26. Kumar Ch S, Sarada P, Reddy Ch S, Reddy M S, Dsv N. Plasma torch toothbrush a new insight in fear free dentisry. J ClinDiagn Res. 2014;8(6):07-10.
27. Fathollah S, Abbasi H, Akhoundi S, Naeimabadi A, Emamjome S. Cold plasma enamel surface treatment to increase fluoride varnish uptake. Sci Rep. 2022;12(1):4657.
28. Jungbauer G, Moser D, Müller S, Pfister W, Sculean A, Eick S. The Antimicrobial Effect of Cold Atmospheric Plasma against Dental Pathogens-A Systematic Review of In-Vitro Studies. Antibiotics (Basel). 2021;10(2):211.
29. Pan J, Sun K, Liang Y, et al. Cold plasma therapy of a tooth root canal infected with enterococcus faecalis biofilms in vitro. J Endod. 2013;39(1):105-110.
30. Armand A, Khani M, Asnaashari M, AliAhmadi A, Shokri B. Comparison study of root canal disinfection by cold plasma jet and photodynamic therapy. Photodiagnosis Photodyn Ther. 2019; 26:327-333.
31. Pavelić B, Švarc MZ, Šegović S, Bago I. Cold atmospheric plasma for bleaching endodontically treated tooth: a new clinical approach. Quintessence Int. 2020;51(5):364-371.
32. Nam SH, Lee HW, Cho SH, Lee JK, Jeon YC, Kim GC. High-efficiency tooth bleaching using non-thermal atmospheric pressure plasma with low concentration of hydrogen peroxide. J Appl Oral Sci. 2013;21(3):265-270.
33. Nam SH, Lee HJ, Hong JW, Kim GC. Efficacy of nonthermal atmospheric pressure plasma for tooth bleaching. Scientific World Journal. 2015; 2015: 581731.
34. Çelik B, Çapar İD, İbiş F, Erdilek N, Ercan UK. Deionized water can substitute common bleaching agents for nonvital tooth bleaching when treated with non-thermal atmospheric plasma. J Oral Sci. 2019;61(1):103-110.
35. Macgregor M, Vasilev K. Perspective on Plasma Polymers for Applied Biomaterials Nanoengineering and the Recent Rise of Oxazolines. Materials (Basel). 2019;12(1):191.
36. Yixin Zhang , Yi Xiong , Peng Xie, Xiaogang Ao, Z heng Zheng, Xiaoqing Dong et al. Non-thermal plasma reduces periodontitis-induced alveolar bone loss in rats.Biochemical and Biophysical Research Communications (BBRC) ;503(3):2040-2046
37. Sato K, Shi L, Ito F, et al. Non-thermal plasma specifically kills oral squamous cell carcinoma cells in a catalytic Fe(II)-dependent manner. J ClinBiochemNutr. 2019;65(1):8-15.
38. Faramarzi F, Zafari P, Alimohammadi M, Moonesi M, Rafiei A, Bekeschus S. Cold Physical Plasma in Cancer Therapy: Mechanisms, Signaling, and Immunity. Oxid Med Cell Longev. 2021;2021:9916796.
39. Whitney LC, Bicanic T. Treatment principles for Candida and Cryptococcus. Cold Spring HarbPerspect Med. 2014;5(6):a024158.
40. Ebrahimi-Shaghaghi F, Atyabi SM, Razzaghi-Abyaneh M. Plasma-based strategy for inhibiting Candida albicans growth and CaMCA1 gene expression in vitro and reducing fungal pathogenicity in a murine model of vulvovaginal candidiasis. Med Mycol. 2021;60(1):myab067.

41. Bekeschus S, von Woedtke T, Emmert S, Schmidt A. Medical gas plasma-stimulated wound healing: Evidence and mechanisms. Redox Biol. 2021;46:102116.
42. Bekeschus S, Kramer A, Schmidt A. Gas Plasma-Augmented Wound Healing in Animal Models and Veterinary Medicine. Molecules. 2021;26(18):5682.