APPLICATIONS OF PLASMA IN MEDICINE

Laura ROMILA[1], Liliana SACHELARIE[2], Mihaela VASILIU[3], Cătălin IOV[1], Agripina ZAHARIA[4] , Nicolae-Tiberiu POPÂRLAN[4], Alexandra BURLUI[6]

[1]Assist. Prof. PhD, „Apollonia" University of Iaşi, Romania
[2]Prof. PhD, „Apollonia" University of Iaşi, Romania
[3]Asoc. Prof. PhD, „Apollonia" University of Iaşi, Romania
[4] Prof. PhD, Ovidius University of Constanşa, Romania
[5]PhD, „Gr.T.Popa" University of Medicine and Pharmacy, Iaşi, Romania
[6]Univ. Assist., PhD Student, „Gr.T.Popa" University of Medicine and Pharmacy, Iaşi, Romania
Corresponding author: Alexandra Burlui; e-mail: alexandra.burlui@yahoo.com

Abstract

This article highlights the fact that lately plasma has gained more and more applications in medicine. Plasma produces both morphological and chemical changes of the surface and free radicals on the polymers' surface. By using various treatments with plasma, changes occur on the surface of some polymer type materials in terms of physical and chemical properties, without affecting their properties as a whole. Plasma-activated water (PAW) is a method well suited for microbiological decontamination treatments. Regarding the biological activity, the plasma activated water presents strong antioxidant features.
Keywords: *surface, treatment, water.*

1. INTRODUCTION

The term plasma medicine refers to the direct treatment of human cells with plasma being the application of plasma physics for therapeutic purpose. In this century, several biological applications of physical phenomena such as X-Rays, MRI Machine, x-ray crystallography were used, all of them providing excellent biomedical information about the human body. For past decade, the effects of plasma on biological specimens were studied more intensively than ever before. It is known that plasma holds great potential to shut down a large variety of microorganisms, which also include Multi-drug resistant (MDR) bacteria, cause angiogenesis (mainly, the formation of new blood vessels), tissue regeneration (formation of new tissues and cells), cell apoptosis (cell death) in mammalian cells showing cancer. This inevitably opens up several fields of research in the area of oncology. Also, in comparison to other radiation therapies like laser therapy, chemotherapy, phototherapy, etc., plasma treatment is considerably safer.

Plasma medicine has been shown to be applicable in following regions:

- Oncology: It is non-invasive and plasma based therapy is targeted. The experimental results on mammals showed little to no side effects (whereas chemotherapy - the current course of action undertaken when a patient suffers from cancer – presents a wide range of side effects such as constant pain, weight loss, considerable immunity loss and WBC count) This is not the case for plasma therapy.
- Wound healing: Plasma medicine also represents a tremendous promise in field of wound healing (especially useful during trauma and emergency medicine where you require quick patching in order to prevent blood loss and accelerate healing). The elevated rates of angiogenesis and tissue regeneration are critical steps in wound healing, which on quickening can ease healing.
- Destroying MDR bacteria: essential for curing MDR bacteria causing diseases.
- Treatment of pathogen based skin diseases and skin decontamination.
- Treatment of chronic and infected wounds by eradicating infection around the area and accelerating healing.
- Another important application is found in dentistry, where one can disinfect root canals in addition to accelerated wound healing of the wounded region. Additionally, one also expects the treatment of intraoral infections

and dental implants to take place shortly after the rather successful clinical trials.
- Possible applications in ophthalmology or plastic surgery are also explored.
- Disinfection with plasma is considered to be fast and efficient within seconds and also benign to the skin.
- It has also been shown to inactivate the spores of the bacteria, which is necessary for epidemic control [1,2].

2. PLASMA AND BIOMATERIALS

The perception of solid materials and particularly of their surfaces is distorted by the limitations of the visible spectrum. The characteristic wavelengths of the photons are 1000 times larger than the dimensions of the surface area, in which the volume properties disappear or are attenuated, granting access to the transition interface with another phase which may be gaseous, liquid or solid [3]. This alteration of the structural and the compositional properties of volume lead to the idea of considering the surface as an additional phase of matter. The surface may be regarded as a layer with variable depth due to wide variation of the surface properties. Different depth regimes play a decisive role in technological applications.

The structure of a surface is often related to its reactivity and composition. The defects that a surface may present such as dislocations, protrusions, edges and corner areas will represent the reactivity centers in the case of a superficial treatment of the surface. In the case of intense or extended treatments on the surface, profound changes in the chemical composition between surface and volume will appear, due to divisions, deposition of particles from the environment and their reaction, surface rearrangements in the first atomic layers and all these changes will lead to the changing of the potential energy of the surface centers [4]. Solid state polymers represent an entity with a precise individualization towards polymers in general. Although the surface layer is about 1% of the polymer's weight, the whole series of events that characterize the properties are manifested through it.

A series of specific features are controlled by the surface of the fibrous polymer as follows:
- The supramolecular structure of the surface involves its accessibility to penetrating the polymer by chemical agents [5];
- The viscoelastic properties of the surface that involves the abrasion and tearing resistance along with the volume ones generate the individual rheological behavior of the polymers and the availability of reagents, eventually colorants.
- The diffusion properties of the chemical agents and dyes (in different processes of preparing, bleaching, dyeing, printing, etc.), where the polymer surface can be modeled as a membrane in which the structure, size and frequency of pores and the thermal level of the glass transition temperature, plays a well-defined role in the availability and selection of the penetrating particles, depending on the properties that characterize the transfer from the liquid to the solid phase;
- The wetting capacity with major implications on the hygiene and physiological properties is due primarily to the chemical structure favoring or remaining inert to humidity adsorption;
- The adhesiveness due to the surface state of polymer; in the current state of knowledge it was highlighted the physical side that has the highest influence, although it is particularly intense studying the chemical aspects involved in adhesion, the processes being complex and difficult to assess [6];
- Electrostatic charge is due to the chemical structure of the polymer and to the free surface energy; the interface may or may not retain the accumulated charges;

By using various treatments the modification of the surface of some polymer type materials in terms of physical and chemical properties succeeded, without affecting their properties as a whole. Therefore, surface treatment of polymer type materials has become an important research area. For this purpose a series of methods are used such as chemical treatment, flame treatment,

treatment through photonic irradiation and plasma treatment. The optimization techniques for modifying the surface through a particular treatment in the case of polymer materials, particularly for textile fibers cannot be made without a deep understanding of the physical and chemical phenomena that occur at their surface in contact with a modification agent, the knowledge of the properties induced in this way being highly necessary [7].

3. THE TREATMENT IN PLASMA MEDIUM

Plasma environments are physical systems that are electrically neutral, comprising electrons, ions, free radicals and neutral molecules and excited particles, produced by the action of high temperatures, strong magnetic fields or electrical discharges in gases. Usually, the luminescent non-destructive electric discharge technique of low or high frequency is being used in gases (air, oxygen, nitrogen, argon) at an appropriate pressure (10^{-2}–10 Torr), using continuous or alternating current and therefore low, medium or completely ionized plasma environments can be obtained. Although gases or gas mixtures may be used, the most widely-used gases for the plasma treatment of polymers are O_2, Ar, H_2, N_2, nitrogen oxides, CF_4 and air. Reactive particles formed in the plasma react directly with the surface, without affecting the mass properties of the treated material [8]. A distinctive characteristic of plasma is the luminous discharge, with colors ranging from blue-white to dark purple, depending on the type of gas. The low pressure processes that occur in the plasma are environmentally friendly and represent an effective way of modifying the surface of the material at the microscopic level. Plasma produces both the morphological and chemical changes of the surface and free radicals on the polymer's surface. For the chemical processing of textiles plasma is used at temperature below 1500^{o}C, respectively "cold" plasma, which excludes the thermal damage of the polymers. The treatment of polymer materials in plasma can produce a superficial corrosion of the surface, cross-linking, activation and deposition of films on the polymer's surface.

Superficial **corrosion** refers to the ability of the plasma to break the polymer's covalent bonds (C-H bonds break easily) by high energy particle bombardment, affecting the majority surface molecular layers of the substrate exposed to the plasma.

Cross-linking is the achievement of chemical bonding between macromolecular chains of the polymer. The plasma processes using inert gas can be used for the polymer's cross-linking and for obtaining a stronger and tougher substrate surface. The transversal bonds formed using plasma treatments provide additional chemical resistance to the materials [9,10].

The activation represents the formation of an optimum number of binding centers at the material's surface. During activation, under the action of plasma, the breaking of the weak bonds from the polymer is produced, and they are replaced by carbonyl, carboxyl, hydroxyl, amino, halogen, reactive groups and other functional groups. Changes occur in their characteristics depending on the type of incorporated groups from the substrate surface. The process of plasma activation through graft polymerization can be used to provide hydrophilic or hydrophobic properties to the substrate.

The deposition refers to the development of coatings (thin films) with various physical properties depending on the nature of the gas from the plasma and the process parameters [11]. The use of low temperature plasma is based on the chemical combination of the surface of the fibrous substrate with the gaseous active species produced in the plasma, having as result the "corrosion" or "exfoliation" effect since the gaseous products of the reaction are removed from the system due to the vacuum that is continuously kept. In a plasma environment, the molecular oxygen is converted into atomic oxygen, the carbon from the substrate into CO or CO_2, the other gases (nitrogen, hydrogen, etc.) being able to induce the formation of new features on the polymer's surface, functions which contain oxygen and are capable of forming hydrogen bonds with water.

In comparison with the traditional techniques, the plasma treatment will be used increasingly more in the future, especially in medicine [12,13].

4. WATER ACTIVATED BY PLASMA

One of the most recent applications of plasma refers to microbiological decontamination. This means for example the ballast water treatment in the maritime field, the preparation of the medical instruments for its use, the cleaning air-conditioning systems, the seed treatment of certain crops in order to avoid further occurrence of pests [2] and so on. This plasma treatment assumes either the direct exposure of the target which is desired to be treated or indirect action by avoiding direct contact. In the latter case, which is preferred for the decontamination treatment or even sterilization, plasma is used to activate a solution (most often distilled water is being used) that will be brought into contact with the target that is desired to be treated [14].

From the point of view of microbiological decontamination treatment efficiency it has been found that maximum efficiency is achieved if microorganisms are suspended (in solution), as compared to the case where they are deposited as biofilm on the solid surface, possibly in multiple layers. For the water's activation, the GlidArc technology was used, which has proven to be the most useful of the non-thermal plasma technologies in order to obtain the desired physical-chemical parameters for the activated water.

The paper presents the neutralization results for some types of microorganisms that can be found both in the ballast water of ships as well as on the medical instruments used in gastroenterology investigation or inside of air-conditioning systems that require regular maintenance operations. Therefore, the presented results are represent a comparison between activated water with plasma and some classical disinfectants type Viruzyme or Virusolve, with a broad coverage spectrum.

Cold plasma can be produced by different types of electrical discharges within laboratory (GlidArc, DBD, Corona) and fits the category of advanced oxidation processes (AOP). The species within it are out of thermodynamic equilibrium, meaning that the energy and temperature of the light particles such as electron and photon type is much higher than the hard particles such as metallic ions [15].

Plasma-activated water (PAW) is a method well suited for microbiological decontamination treatments, both due to the chemical species that it contains, and to the fact that the reactions induced continue for a relatively long period of time (TPDR effect). The fact that the microbiological target which is intended to be treated is not the subject of direct effect of the plasma action offers another major advantage and that is to avoid the possibility of additional contamination of the target due to the blowing gas necessary to produce GlidArc. Previous studies [16] demonstrated that through activated water a reduction up to 10 logarithmic units of colony-forming can be obtained.

Plasma-activated water (PAW) enables the development of the smallest number of microorganisms for times up to 10 hours. After this time, in which PAW is proved to be the most effective decontamination agent, one can observe that the sample treated with Viruzyme has the lowest number of microorganisms, the results being comparable with the sample treated with PAW. By using plasma-activated water as a decontamination agent the microbiological results are better than in the case of using other classic decontamination agents for a time up to 12 hours after the decontamination process. Also, the maximum efficiency of PAW's use is obtained after a period of 10-12 hours, but the effect continues up to 24 hours. The necessary time for the activation of plasma is about 8 minutes. One could observe, for this period of time, the obtaining of a pH corresponding to the initiation of the chemical reaction and neutralization of microorganisms.

All these indicators of time or mixing proportions for PAW/seawater are available to reactor resources and power supply sources in the research laboratory. Prior to this comparative study, tests with PAW were carried out and a reduction of 3 logarithmic units of the initial number of microorganisms in the solution to be treated was obtained. Therefore, by optimizing the existing resources, an improved efficiency can be achieved, which allows the practical implementation of this decontamination method [17].

Water treatment by direct electrical discharges may provide a means to utilize these species in addition to ozone. More research and development activity has been devoted to achieve these targets in the recent past. An overview of these techniques and important developments that have taken place in this area are discussed. In particular, pulsed corona discharge, dielectric barrier discharge and contact glow discharge electrolysis techniques are being studied for the purpose of cleaning water. The units based on electrical discharges in water or close to the water level are being tested at industrial-scale water treatment plants [18].

In order to create Plasma Activated Water, water is electrolyzed using plasma while in a container with normal air. The creation of this antimicrobial water sparked an interest in its many uses. Along with producing acidic water solutions, an altered version of this process can create alkaline water with antioxidant properties, used to help prevent cells from oxidation via free radicals [19].

Features of Plasma Activated Water (PAW)

There are studies that showed that the acquired features of PAW have a long shelf life (PAW keeps the acquired features up to 24 month and are relatively stable towards external influences. Regarding the biological activity the plasma activated water presents strong antioxidant features (at microbiological level). PAW improves intercellular metabolism. Another feature is the property to facilitate impact (effect) of pharmaceuticals when applied in combination with PAW or even terminating antibiotic resistivity. There are modes of activation when PAW acquires properties of Bacteria, virus and Fungi growth stimulation feature because PAW is in symbiosis with a wide spectrum of enzymes [20].

Some results for *E. coli* and *P. aeruginosa*, reveal the following:

a. The *Effect of Plasma activated water on the viability of E. coli over time*: after just 15 min incubation in activated water, the number of bacteria was reduced by 99.5% compared to controls [9]. They were no longer viable after 24 h of incubation in activated water. Thus, activated water was highly effective at killing this E. coli strain.
b. The *Effect of Plasma activated water on the viability P. aeruginosa over time*: after 24 h, the control sample contained 5 x 107 cells/ml and the activated water sample contained 5 x 106 cells/ml.
c. *Plasma activated water increased the sensitivity of P. aeruginosa to low levels of antibiotics* : Pseudomonas aeruginosa is not very sensitive to many commonly used antibiotics, including ampicillin and kanamycin. However, these antibiotics are affective against many other bacteria including E. coli.

Activated water appears to greatly enhance the effectiveness of certain antibiotics in killing bacteria like P. aeruginosa, which is very difficult to eradicate due to its intrinsic antibiotic resistance.

Possible ways and areas of plasma activated water usage:

- As "activator" of wide spectrum of pharmaceuticals, including antibiotics;
- As base for physiological (salt) solutions and injections;
- For vaccines preparation;
- As "transport platform" for medication;
- As antibiotic, anti-fungi and anti-virus pharmaceutical;
- As pharmaceutical (in combination with or without other pharmaceuticals) in treatment of:
  - Burns of different origin;
  - Wounds, ulcers, sores and other skin diseases;
  - Inflammation of internal organs.
- As stimulator of Bacteria and Fungi growth (for BioTech);
- As disinfectant (in liquid, vapor and frozen state), that does not affect surfaces/materials/tissue under disinfection [21].

Water Purification by Electrical Discharges

Water treatment by direct electrical discharges may provide a means to use these species in addition to ozone. Much research and development activity has been devoted to achieving these targets in the recent past. An overview of these techniques and important developments that have taken place in this area are presented. In particular, pulsed corona discharge, dielectric barrier discharge and contact glow discharge electrolysis techniques are being studied for the purpose of cleaning water [18]. The units based on electrical discharges in water or close to the water level are being tested at industrial-scale water treatment plants.

Something happens to water when you spray it through an electrical field: the water can now fight microbes. Paul Leenders claims that it makes crops grow faster with greater yield while eliminating the need for pesticides. Another use for plasma in relation to purifying water is creating ozone; with UV light, both can be used to create ozone from oxygen which can kill bacteria in water [22].

a. Because science is never done

A Chinese team recently reported that soaking button mushrooms in plasma-activated water reduced counts of bacteria and fungus and helped keep the mushrooms fresher. A German team has been designing tests that could establish PAW's suitability for sterilization in medical settings. A Russian team published a paper in 2011 showing that PAW promoted germination and root growth in zinnia flowers. Meanwhile, an American team found that, oddly, a 15-minute exposure to PAW killed more *E. coli* bacteria suspended in the water than did a three-hour exposure [17].

b. PAW as a disinfectant

Many studies were focused on comparing PAW to other disinfectants such as alcohol. Cheap, widely accessible disinfectants are particularly valuable in hospitals because they can play a role in reducing infections. Around 7% of hospitalized patients acquire a new infection during treatment; in the developing world the number is 10 %, according to estimations made by the World Health Organization. Therefore PAW can provide a useful alternative to the existing disinfectants [17,23]. A study conducted by Ma et al. focused on the non-thermal plasma-activated water inactivation of food-borne pathogen on fresh produce. In their research, they demonstrated how Plasma Activated Water could be used in order to reduce food-borne bacteria [24].

c. PAW as a preservative

Food companies are interested in using PAW or other plasma-activated solutions to preserve food. Short bursts of plasma-activated air helped decontaminate chicken in a 2011 study. Meanwhile, FloraHolland, a flower growers' cooperative in The Netherlands, has been working with Leenders to test university-produced samples of PAW in order to store cut flowers - in the place of the chlorinated water typically used [20].

d. PAW on the farm

Leenders dreams of farmers using PAW to spray their crops, to enhance growth (containing ammonia, it can be a natural fertilizer) and cut down on harmful microbes in the soil. Large-scale usage is still a long way off — his current machine only produces around 120 liters an hour, which is quite enough for one hectare of farmland. And as another caveat: PAW doesn't actually fend off insects, so farmers would still need a treatment to do that. Given the regulatory challenges of getting a product approved as a biocide, fungicide, or pesticide, Leenders says it may make more sense to start with plant growth enhancement first [23].

5. CONCLUSIONS

Although plasma activated water is a remarkable discovery, reverse osmosis and distillation are still probably the most effective and widespread methods of purifying water [19]. Some believe that using plasma activated water in conjunction with other forms of purification might be the most effective option yet. After some experimentation, Leenders' theory proved to be more than just a hunch. While it still has a long road of testing and verification ahead of it, this innovative concept provides us with a peak into what the future might hold as we attempt to correct our ecologically devastating habits.

Scientists around the world are looking at PAW in a fast-developing field, which tests a broad range of uses. They hope to harness PAW to fight microbes in hospitals and on farms. They also hope that this development, or something similar, could prove to be a viable alternative to current methods, which have turned out to have a devastating ecological impact. Yet, regardless of whether we see Plasma Activated Water becoming a revolutionary technology or not, it is undeniably a fascinating phenomenon worthy of our study.

References

1. Plasmatreat. Plasma medicine – can the direct application of Openair® plasma heal wounds? [Internet] Elgin, Moray [cited 2018 November 15]. Available from: https://www.plasmatreat.com/industrial-applications/life-sciences/plasma-medicine.html
2. Dr Hempel network. Plasma medicine. Applications, companies & market [Internet] Dusseldorf [cited 2018 November 15]. Available from: https://www.dr-hempel-network.com/digital-health-technolgy/plasma-medicine-applications-companies-market/
3. Corke TC, Enloe CL, Wilkinson SP. Dielectric barrier discharge plasma actuators for flow control. Annu Rev Fluid Mech. 2010;42(1):505-29.
4. Sera B, Gajdova I, Sery M, Spatenka P. New physicochemical treatment method of poppy seeds for agriculture and food industries. Plasma Sci Technol. 2003;15(9):935. DOI : 10.1088/1009-0630/15/9/19.
5. Richard F, Cormier JM, Pellerin S, Chapelle J. Physical study of gliding arc discharge. J. Apps Phys. 1996;79(5):2245-50.
6. Brelles-Marino G, ed. Biological and environmental applications of gas discharge plasmas. Pomona: Nova Science Publisher;2009.
7. JSC "TECHNOSYSTEM-ECO" Moscow, Russia. Utilization of plasma activated water in biotechnology, Pharmacology and Medicine. [Internet] Ost-West-Wissenschaftszentrum;2009 [cited 2018 November 7]. Available from: http://www.owwz.de/fileadmin/Biotechnologie/BioVeranst/Online_Presentation_2009/Bakhar.pdf
8. Pai K, Timmons C, Roehm KD, Ngo A, Narayanan SS, Ramachandran A, Jacob JD, Ma LM, Madihally SV. Investigation of the roles of plasma species generated by surface dielectric barrier discharge. Sci Rep. 2018;8(1):16674.
9. Joshi SG, Cooper M, Yost A, Paff M, Ercan UK, Fridman G, Friedman G, Fridman A, Brooks AD. Nonthermal dielectric-barrier discharge plasma-induced inactivation involves oxidative DNA damage and membrane lipid peroxidation in Escherichia coli. Antimicrob Agents Chemother. 2011;55(3):1053-62.
10. Chan CM. Polymer Surface, Modification and Characterization. Munich, Viena, New York: Hanser Publisher;1994.
11. Weltmann KD, Polak M, Masur K, Von Woedke T, Winter J, Reuter S. Plasma Processes and Plasma Sources in Medicine. Contrib Plasm Phys. 2012;52(7):644-54.
12. Ermolaeva SA, Sysolyatina EV, Kolkova NI, Bortsov P, Tuhvatulin AI, Vasiliev MM, Mukhachev AY, Petrov OF, Tetsuji S, Naroditsky BS, Morfill GE, Fortov VE, Grigoriev AI, Zigangirova NA, Gintsburg AL. Non-thermal argon plasma is bactericidal for the intracellular bacterial pathogen Chlamydia trachomatis. J Med Microbiol. 2012;61(Pt 6):793-9.
13. Ermolaeva SA, Varfolomeev AF, Chernukha MY, Yurov DS, Vasiliev MM, Kaminskaya AA, Moisenovich MM, Romanova JM, Murashev AN, Selezneva II, Shimizu T, Sysolyatina EV, Shaginyan IA, Petrov OF, Mayevsky EI, Fortov VE, Morfill GE, Naroditsky BS, Gintsburg AL. Bactericidal effects of non-thermal argon plasma in vitro, in biofilms and in the animal model of infected wounds. J Med Microbiol. 2011;60(Pt 1):75-83.
14. Prokhorova P. Utilization of plasma activated water in Biotechnology. Moscow, Russia: Pharmacology and Medicine;2009.
15. Thirumdas R, Kothakota A, Annapure U, Siliveru K, Blundell R, Gatt R, Valdramidis VP. Plasma activated water (PAW): Chemistry, physico-chemical properties, applications in food and agriculture. Trends Food Sci Technol. 2018;77:21-31.
16. 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). doi: 10.3791/56331.
17. Heinlin J, Isbary G, Stolz W, Morfill G, Landthaler M, Shimizu T, Steffes B, Nosenko T, Zimmermann J, Karrer S. Plasma applications in medicine with a special focus on dermatology. J Eur Acad Dermatol Venereol. 2011;25(1):1-11.
18. Tanaka H, Hori M. Medical applications of non-thermal atmospheric pressure plasma. J Clin Biochem Nutr. 2017;60(1):29-32.
19. Kaushik NK, Ghimire B, Li Y, Adhikari M, Veerana M, Kaushik N, Jha N, Adhikari B, Lee SJ, Masur K, von Woedtke T, Weltmann KD, Choi EH. Biological and medical applications of plasma-activated media, water and solutions. Biol Chem. 2018;400(1):39-62.
20. Adachi T. Introduction to serial reviews: Biomedical application of non-thermal atmospheric pressure plasma and its usefulness. J Clin Biochem Nutr. 2017;60(1):1-2.
21. Choi JS, Kim J, Hong YJ, Bae WY, Choi EH, Jeong JW, Park HK. Evaluation of non-thermal plasma-induced anticancer effects on human colon cancer cells. Biomed Opt Express. 2017;8(5):2649-59.
22. Haertel B, von Woedtke T, Weltmann KD, Lindequist U. Non-thermal atmospheric-pressure plasma possible application in wound healing. Biomol Ther (Seoul). 2014;22(6):477-90.
23. Won HR, Kang SU, Kim HJ, Jang JY, Shin YS, Kim CH. Non-thermal plasma treated solution with potential as a novel therapeutic agent for nasal mucosa regeneration. Sci Rep. 2018 Sep 13;8(1):13754.
24. Ma R, Wang G, Tian Y, Wang K, Zhang J, Fang J. Non-thermal plasma-activated water inactivation of food-borne pathogen on fresh produce. J Hazard Mater. 2015;300:643-51.