Journal of New Materials for Electrochemical Systems

Vol. 24, No.4, October 2021, pp. 293-296

Journal homepage: http://iieta.org/journals/jnmes

Potential Application of Picosecond Pulsed Electric Field (PPEF): Advanced Bioelectrical Technology for Potential COVID-19 Treatment

Ahmad Reza Farmani [1,2], R James Swanson [3*], Forough Mahdavinezhad [4], Mohammad Hasan Shoormeij[5],
Sadegh Mohammadi [6], Alaa Moeinzadeh[7, 8], Fatemeh Ghazipour[9], Jafar Ai [1*]

[1]Tissue Engineering and Applied Cell Sciences Department-School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran.
[2]Tissue Engineering Department-School of Advanced Technologies in Medicine, Fasa University of Medical Sciences, Fasa, Iran.
[3]Department of Anatomical Sciences, College of Osteopathic Medicine, Liberty University, Lynchburg, Virginia, United States of America (USA).
[4]Anatomy Department-School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
[5]Emergency Medicine Department, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
[6]Department of Plastic Engineering, Faculty of Polymer Processing, Iran Polymer and Petrochemical Institute, Tehran, Iran.
[7]Department of Anatomical Sciences, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
[8]Cellular and Molecular Research Center, Iran University of Medical Sciences, Tehran, Iran.
[9]Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Corresponding Author Email: jafar_ai@tums.ac.ir

https://doi.org/10.14447/jnmes.v24i4.a10

Received: August 17-2020
Accepted: September 30-2021

Keywords:
COVID-19, Picosecond Pulsed Electric Field (PPEF), Picotechnology, NAIs, Subsidiary Treatment, Advanced Technology.

ABSTRACT

As human knowledge has increased, the efficacy and precision of tools to solve clinical problems have also increased. The challenge of COVID-19 has posed a significant threat to human life and reflects the need to upgrade existing technologies and make treatments more precise. Since the corona virus particle is in the nanometer range, the need for a device with accuracy beyond the nanometer range is apparent to control and eliminate it. Using Picosecond Pulsed Electric Fields (PPEF) could be a good antiviral picotechnology candidate. PPEF energy can (1) increase the innate immunity function of polymorphonuclear neutrophils, (2) destroy bacteria and other pathogens, and (3) potentially inactivate viral particles. This characteristic of PPEFs has already been used in the food industry. Both PPEF and nanosecond PEF technology is being used to treat cancer in research animals and has reached the stage of pre-clinical and clinical human trials with use in clinical practice soon to follow. Applying advanced PPEF technology against COVID-19 should provide new opportunities for effective human antiviral treatment.

.

1. PROOF OF CONCEPT

This is note on a proof of concept which is suggested to treat COVI-19. Accordingly, it is not presented in a standard form of the classic research papers. Based on the impact of COVID-19 on our lives these years we present here an original concept for its treatment.

Bottom-up designing, i.e., starting with the individual base elements of a system and then linking these elements together to form larger subsystems until a complete top-level system is formed, is a strategy often used in scientific research. This perspective gives initial control over the basic conceptual elements and, over the last few decades, led scientists to ultimately develop nanotechnology. This technology has brought dramatic advances in various fields of science, including medicine. This progress has reduced the prevalence of pathogens, especially bacteria, advanced the wound-healing process, and caused apoptosis and/or necrosis of certain carcinomas [1]. All these various effects seem to be accomplished through disruption of the microstructure, and thus function, of the cell membrane, the intracellular organelle contents, the membranes surrounding the intracellular organelles, or, more likely, a combination of these structural and functional characteristics. These changes could include aberrations in DNA, RNA, and proteins. Emergence of the new coronavirus with its nanometer-size, poses a serious threat to the health and economy of human society. In order to combat viruses, especially the COVID-19 virus, attention to picotechnology could uncover the means for controlling viral structure and function at the atomic and molecular-sized levels, making COVID-19 virus's demise inevitable [2, 3].

However, as far as we know this viral infection mainly targets the lower respiratory system leading to acute respiratory distress syndrome (ARDS), and hyperinflammation which may lead to death [4, 5]. This disease not only targets the respiratory system but is also related to hyper inflammation creating multi-organ damages [6]. Several approaches for combating COVID-19, including vaccines, antiviral drugs, herbal medicine, and monoclonal antibodies have been presented [3, 7, 8]. Despite all of the efforts, the main role of survival of patients is still related to the immune system of patients [9, 10]. Moreover, new variants of the SARS-COV2 virus including delta, and lambda have created many challenges to therapeutic approaches and the efficiency of vaccines [11, 12]. Hence, trying to find new strategies for overcoming this challenging problem is crucial, and biophysics may help us solve the problem from a new perspective [13, 14]. Bioelectricity is one of the known novel areas of biophysics that can control cell behaviors by electrical and electrochemical stimulations [15].

Polar ions, molecules, and structures functioning in a biological milieu within the cells makes them perfect candidates for manipulating by application of an electrical field, and especially by pulsed electric fields [16, 17]. Pulsed electric fields (PEF) have been used for military applications, the food industry, and water treatment, with the latter two including health applications based on PEF's ability to remove a variety of pathogens [18]. Original PEF development used milli- and micro-second pulses that produced cellular electroporation. This technology created permeable pores in the cell membrane. Formation of aqueous membrane pores lead to reversible electroporation (REP), electrofusion (EF), and irreversible electroporation (IEP). PEF also affects biomolecules by non-thermal mechanisms and induces DNA nicking, which affects the integrity of DNA molecules.

Moreover, a PEF could either decrease or increase cellular enzymatic activities which could lead to the formation of new genes [19, 20]. Exposing microorganisms to a high PEF in the vegetative state could lead to temporary or long-term destabilization of both structure and function. PEFs can alter the permeability of the cell's membrane that can alter its ability to modulate the movement of molecular and ion passage across the cell membrane. Changing the threshold value can lead to swelling and eventual lysis of the microorganisms' membrane [21]. Although, this lysis could be the main mechanism of disinfection by PEF application, reducing the pulse duration from the nanometer level to the picometer level might open up a new field of investigation. This thousand-fold decrease in pulse duration could stimulate modification of important ions, for example intracellular Ca2+ mobilization, and should be investigated [22]. Basically, in the ultrashort pulses, the major cause of cell death is damaging of the intracellular structures such as the nucleus, and not the breaking down of the outer membrane. Thus, short duration, high-voltage pulses with appropriate electric field strengths could have a strong deleterious effect on microorganisms [21]. The main parameters determining the efficiency of PEF disinfection are the voltage strength and pulse duration. Other important factors include cell size and shape, membrane structure/function, and the growth stage of the microorganisms being treated for optimum disinfection [23]. Despite all the research which has been published on bacterial disinfection by PEF, especially in food preservation, there are no publications assessing its effect on viruses [24-27]. Research implies that larger field's strength is required to alter intracellular organelles of smaller cells and microorganism like viruses [28]. Therefore, applying high voltage pulses with low duration could be the right choice for incapacitating viruses, and picosecond pulsed electric fields (PPEF) with high voltage could be an even better tool.

The relatively long survival of COVID-19 viral particles in different environments, its high infectivity, and prevalence, has caused great global concern. Given the presence of the virus in human feces drives the need for pulsed electric field technology in cleaning environmental water in wastewater treatment. Nanosecond (NS) PEF or PPEF could be the key to improving environmental conditions and eliminate viruses from the environment during this pandemic [29]. Using a conducting nanosponge with pulsed electric filed to create a new, affordable, and highly efficient treatment for disinfection of microorganisms in water by electroporation through NSPEF or PPEF [30].

A number of recent publications support the amazing, positive results with the use of NSPEFs or PPEFs. NSPEF or PPEF technology has been used in cancer treatment. Part of this treatment success is due to the nanosecond and picosecond pulsed electric fields ability to amplify the function of the immune system, specifically the neutrophil. These PEFs produce apoptosis of cancer cells and reduce angiogenesis [31, 32]. Wound disinfection has been successful when using high-voltage, short PEFs [33], by applying transcutaneous electric pulses through two-plate electrodes placed on either side of the tibial muscle in a mouse leg. The immunogenicity of an influenza DNA vaccine was shown to increase after intramuscular injection in the mouse [34]. In citing these various publications, the implementation of this technology is suitable for many applications with variable electrodes, voltages, and pulse duration. The physical property distinguishing between normal and cancerous cells is that tumor cells have different dielectric properties which have a strong effect on the response to PEFs [35]. A similar trend might exist between normal and virally infected cells. This potential difference needs to be examined in further studies. Considering the similarities between viral replication in virally infected cells, and cancer cell DNA replication, applying PEF technology against viral infection is a theory bolstered by excellent logic. We propose that virally infected cells could be eliminated using PEF technology with the progression of viral infection be disrupted. PEF, and especially PPEF, can improve the immunogenicity of immune cells against pathogens and cancer. Research shows that PEFs can induce creation of negative air ions (NAI) leading to a decrease in serotonin levels resulting in immune system activation, specifically NK-cells against viral pathogens. NAIs lead to better tissue oxygenation and eliminate airborne viruses. This can help overcome COVID-19 [36, 37]. Thus, PPEF could be an excellent candidate for ancillary treatment, in addition to vaccines, and would additionally improve the hospital environment. The potential mechanism for the benefits of using PPEF technology for coping with COVID-19 infection is shown in figure 1.

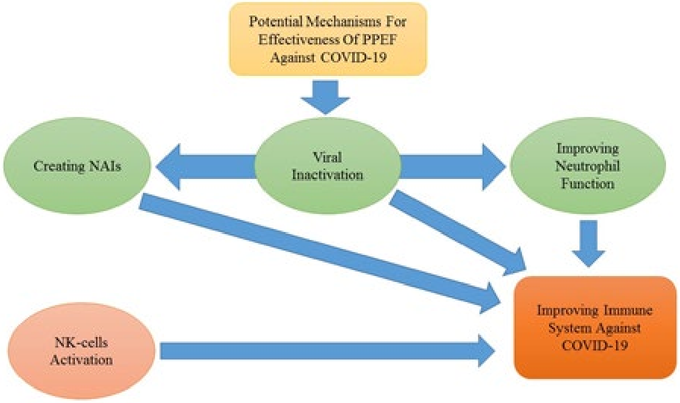

Figure 1. Potential mechanism for the advantage of applying PPEF to COVID-19

2. CONCLUSION

Based on the key role of the immune system in preserving the lives of COVID-19 patients, coupled with the antiviral potential for this technology, using nanosecond, or picosecond pulsed electric field treatment could be an effective adjunct therapy for COVID-19 patients. Due to the historical application of this technology in the food industry, water processing, and wastewater treatment, paying more attention to its use for viral disinfection could play a major role in improving the quality of human life in special conditions related to the new coronavirus disease. This would improve the quality of human life in this current worldwide pandemic state.

REFERENCES

[1] Schoenbach, K.H., et al., Bioelectric effects of intense nanosecond pulses. IEEE Transactions on Dielectrics and Electrical Insulation, 2007. 14(5): p. 1088-1109.
[2] Rabiee, N., et al., COVID-19 and Picotechnology: Potential Opportunities. Medical Hypotheses, 2020: p. 109917.
[3] Farmani, A.R., et al., Anti-IgE monoclonal antibodies as potential treatment in COVID-19. Immunopharmacology and Immunotoxicology, 2021. 43(3): p. 259-264.
[4] Swenson, K.E. and E.R. Swenson, Pathophysiology of ARDS and COVID-19 Lung Injury. Critical Care Clinics, 2021.
[5] Gustine, J.N. and D. Jones, Immunopathology of Hyperinflammation in COVID-19. The American Journal of Pathology, 2021. 191(1): p. 4-17.
[6] Tyagi, S.C. and M. Singh, Multi-organ damage by covid-19: congestive (cardio-pulmonary) heart failure, and blood-heart barrier leakage. Molecular and Cellular Biochemistry, 2021. 476(4): p. 1891-1895.
[7] Alnefaie, A. and S. Albogami, Current approaches used in treating COVID-19 from a molecular mechanisms and immune response perspective. Saudi Pharmaceutical Journal, 2020. 28(11): p. 1333-1352.
[8] Silveira, D., et al., COVID-19: Is There Evidence for the Use of Herbal Medicines as Adjuvant Symptomatic Therapy? Frontiers in pharmacology, 2020. 11: p. 581840-581840.
[9] Brodin, P., Immune determinants of COVID-19 disease presentation and severity. Nature Medicine, 2021. 27(1): p. 28-33.
[10] Schultze, J.L. and A.C. Aschenbrenner, COVID-19 and the human innate immune system. Cell, 2021. 184(7): p. 1671-1692.
[11] Chen, J. and H. Lu, New challenges to fighting COVID-19: Virus variants, potential vaccines, and development of antivirals. BioScience Trends, 2021. advpub.
[12] Ng, Y.L., C.K. Salim, and J.J.H. Chu, Drug repurposing for COVID-19: Approaches, challenges and promising candidates. Pharmacology & Therapeutics, 2021. 228: p. 107930.
[13] Nurmemmedov, E., et al., Biophysics of viral infectivity: matching genome length with capsid size. Quarterly reviews of biophysics, 2007. 40(4): p. 327-356.
[14] Barrantes, F.J., The Contribution of Biophysics and Structural Biology to Current Advances in COVID-19. Annual Review of Biophysics, 2021. 50(1): p. 493-523.
[15] Schofield, Z., et al., Bioelectrical understanding and engineering of cell biology. Journal of The Royal Society Interface, 2020. 17(166): p. 20200013.
[16] Tasoglu, S., et al., Manipulating biological agents and cells in micro-scale volumes for applications in medicine. Chemical Society Reviews, 2013. 42(13): p. 5788-5808.
[17] Chu, P.-Y., et al., The Influence of Electric Parameters on the Manipulation of Biological Cells in a Microfluidic System Using Optically Induced Dielectrophoresis. Int. J. Electrochem. Sci, 2019. 14: p. 905-918.
[18] Buchmann, L. and A. Mathys, Perspective on Pulsed Electric Field Treatment in the Bio-based Industry. Frontiers in bioengineering and biotechnology, 2019. 7: p. 265.
[19] Golberg, A., The impact of pulsed electric fields on cells and biomolecules: Comment on "Lightning-triggered electroporation and electrofusion as possible contributors to natural horizontal gene transfer" by Tadej Kotnik. Physics of Life Reviews, 2013. 10(3): p. 382-383.
[20] Schoenbach, K.H., et al., Bacterial decontamination of liquids with pulsed electric fields. IEEE Transactions on Dielectrics and Electrical Insulation, 2000. 7(5): p. 637-645.

[21] Narsetti, R., et al., Microbial inactivation in water using pulsed electric fields and magnetic pulse compressor technology. IEEE transactions on plasma science, 2006. 34(4): p. 1386-1393.

[22] Semenov, I., S. Xiao, and A.G. Pakhomov, Primary pathways of intracellular Ca2+ mobilization by nanosecond pulsed electric field. Biochimica et Biophysica Acta (BBA)-Biomembranes, 2013. 1828(3): p. 981-989.

[23] Syed, Q., et al., Pulsed electric field technology in food preservation: A review. Journal of Nutritional Health & Food Engineering, 2017. 6(6): p. 168-172.

[24] Wang, M.-S., et al., A review of sublethal effects of pulsed electric field on cells in food processing. Journal of food engineering, 2018. 223: p. 32-41.

[25] Mizuno, A., et al. Inactivation of viruses using pulsed high electric field. in Conference Record of the 1990 IEEE Industry Applications Society Annual Meeting. 1990. IEEE.

[26] Sakudo, A., T. Onodera, and Y. Tanaka, Inactivation of viruses.

[27] Hirneisen, K.A., et al., Viral inactivation in foods: a review of traditional and novel food-processing technologies. Comprehensive Reviews in Food Science and Food Safety, 2010. 9(1): p. 3-20.

[28] Hart, F.X. and J.R. Palisano, The application of electric fields in biology and medicine, in Electric Field. 2017, IntechOpen.

[29] Heller, L., C.R. Mota, and D.B. Greco, COVID-19 faecal-oral transmission: Are we asking the right questions? Science of the Total Environment, 2020: p. 138919.

[30] Liu, C., et al., Conducting nanosponge electroporation for affordable and high-efficiency disinfection of bacteria and viruses in water. Nano letters, 2013. 13(9): p. 4288-4293.

[31] Koga, T., et al., Nanosecond pulsed electric fields induce extracellular release of chromosomal DNA and histone citrullination in neutrophil-differentiated HL-60 cells. Scientific reports, 2019. 9(1): p. 1-13.

[32] Wu, L., et al., The effects of a picosecond pulsed electric field on angiogenesis in the cervical cancer xenograft models. Gynecologic oncology, 2016. 141(1): p. 175-181.

[33] Golberg, A., et al., Pulsed electric fields for burn wound disinfection in a murine model. Journal of Burn Care & Research, 2015. 36(1): p. 7-13.

[34] Bachy, M., et al., Electric pulses increase the immunogenicity of an influenza DNA vaccine injected intramuscularly in the mouse. Vaccine, 2001. 19(13-14): p. 1688-1693.

[35] Sundararajan, R., Electroporation-based therapies for cancer: From basics to clinical applications. 2014: Elsevier.

[36] Jiang, S.-Y., A. Ma, and S. Ramachandran, Negative air ions and their effects on human health and air quality improvement. International journal of molecular sciences, 2018. 19(10): p. 2966.

[37] Herr, N., C. Bode, and D. Duerschmied, The effects of serotonin in immune cells. Frontiers in cardiovascular medicine, 2017. 4: p. 48.