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Application of Atmospheric Microplasma for Nose to Brain Drug Delivery

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ABSTRACT

Intranasal drug administration has emerged as a promising non-invasive approach to bypass the BBB and facilitate direct nose-to-brain (N2B) transport of drugs. This route exploits the unique anatomical connection between the nasal cavity and the brain, enabling therapeutic compounds to reach the central nervous system (CNS) with reduced systemic exposure [1]. However, nasal physiology can hinder drug absorption and limit bioavailability. To address this limitation, we explored the application of a novel spiral-wound dielectric barrier discharge (DBD) microplasma device to enhance the nose-to-brain delivery of therapeutic. Previous studies have shown an improvement in the use of DBD microplasma for biomedical application including transdermal drug delivery [2], but little to no report for its use in brain drug delivery.

This study investigated the effect of DBD microplasma treatment to enhance the brain delivery of galantamine hydrobromide (MW: 368.27 Da), a therapeutic agent commonly used in treatment of neurodegenerative disorders. Utilizing 8-week-old male Sprague Dawley (SD) rats, purchased from Japan SLC Inc, we designed a minimally invasive protocol where anesthetized rats placed in supine position received plasma treatment via insertion of the DBD microplasma electrode into the left nostril, followed by intranasal administration of 10 µL (~0.36 mg) galantamine in divided doses of 2 µL, alternating between the left and right nostril (Fig 2). The time interval between each dose is 10 seconds and rat remained in supine position for 10 minutes. After additional one hour in cage, rats were sacrificed. Brain and nasal mucosa were harvested and cryopreserved for analysis. The experiment complied with regulations for Care and Use of laboratory Animals of Hamamatsu University School of Medicine, Japan.

The DBD device consisted of a high-voltage copper electrode coated with a dielectric barrier and a spirally wound ground electrode. The device generates reactive species upon activation. These species are hypothesized to transiently alter the nasal epithelium, thereby enhancing drug permeability.

To assess drug biodistribution, we employed Matrix-Assisted Laser Desorption Ionization-Imaging Mass Spectrometry (MALDI-IMS), enabling spatial visualization of galantamine across tissues. Galantamine was detected at a mass-to-charge ratio (m/z) of 288.16 Da, and results revealed a markedly higher accumulation of drug in both brain hemispheres of plasma-treated rats compared to non-plasma treated controls (Fig 3). Interestingly, although plasma treatment was applied only to the left nostril, bilateral brain distribution was observed, suggesting systemic CNS access via both olfactory and trigeminal pathways.

These findings provide strong evidence that DBD microplasma facilitates N2B transport of small-molecule drugs. The enhanced uptake is likely due to temporary modulation of the nasal barrier function by reactive plasma species, allowing improved diffusion and absorption of galantamine into the brain. To our knowledge, this is the first report demonstrating the successful application of a DBD microplasma device for enhancing intranasal brain drug delivery.

Future studies will explore the underlying molecular mechanisms and long-term safety of repeated plasma exposure to the nasal cavity.

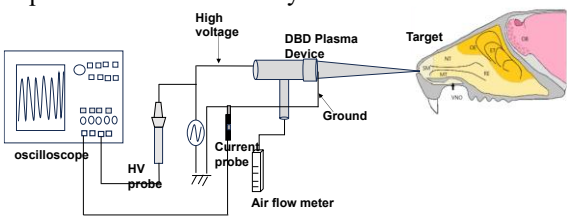

Fig 1: Schematic diagram of the DBD microplasma set-up

Fig 2: DBD microplasma device energized in room air showing the radiative state of plasma discharge.

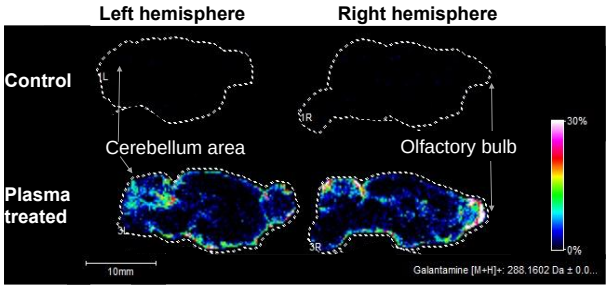

Fig 3: MALDI ion images showing high galantamine detection in olfactory bulb and cerebellum of both left and right brain hemisphere of plasma treated rat compared to control rat.

References

[1] Lofts A, Abu-Hijleh F, Rigg N, Mishra RK, Hoare T. Using the Intranasal Route to Administer Drugs to Treat Neurological and Psychiatric Illnesses: Rationale, Successes, and Future Needs. CNS Drugs. 2022. 36(7):739-770.

[2] Shimizu, K.; Kristof, J. Microplasma Drug Delivery. In Plasma Medicine—Concepts and Clinical Applications; InTechOpen Publisher: Rijeka, Croatia, 2018