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Short research communication

Biological nanoaerosols: from delivering drugs to collecting lung liquid in exhaled air

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Abstract

Lung cancer is the leading cause of cancer deaths, resulting in the loss of over 1.5 million lives world-wide each year. The current treatment is ineffective with a five-year survival rate of below 18%. This short research communication intended to introduce a novel approach and device recently developed in our laboratory, which can be used for early detection and more effective interventions of lung cancer.

Short research communication

Nanoaerosolized drugs (ND) have attracted much attention recently due to their numerous potential benefits. First, due to their size, ND penetrate deep into alveolar regions where they become available for phagocytosis by alveolar macrophages while avoiding mucociliary clearance. Second, ND are expected to have different mechanisms of action and are predicted to require reduced doses for treatment. Some published studies already support the idea that effective doses for ND are significantly reduce das compared to the oral route [1].

Further studies in this area have highlighted substantial technical problems with both the generation of ND from fragile

科研简报

生物纳米气溶胶：从递送药物到从呼出的空气收集肺液

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摘　要

肺癌是癌症死亡的最主要元凶；每年在世界范围内夺去一百五十多万人的性命。目前对肺癌的治疗效果欠佳：五年的存活率低于 18%。本文旨在介绍本实验室最近研发出的一种新方法与装置，其可望用于肺癌的早期检测，以及促进更有效的治疗

科研简报

由于其众多的潜在应用价值， 纳米雾化药物（ND）最近已经吸引了很多关注。首先，由于它们的分子量极小，ND 可避免遭粘膜纤毛清除，而深入渗透到肺泡部位。在肺泡区域，ND 可被肺泡巨噬细胞吞噬。而被肺组织利用。第二，已有人预测：ND 可有不同的作用机制，并可减少治疗药量。 近期发表的研究资料支持这一预测：与口服剂量相比，ND 的用药量显著减少[1]。

然而，进一步研究揭示：开发 ND 面临两大技术问题挑战： 1. 如何用脆弱的生物分子生

biological molecules and measurements of the inhaled doses. To meet these challenges, we developed a new technology and device for the mild atomization of biologically active substances based on the gas-phase neutralization of electrosprayed solutions and a special ND dosimeter [2]. Figure 1 illustrates the general view of the generator along with its principle of operation.

产 ND；2. 如何测量吸入的剂量。为应对这些挑战，我们开发了一种可测量适度雾化的生物活性物质的新技术和设备。此新技术和设备基于电喷雾溶液的气相平衡，以及一个特殊 ND 放射性剂量仪 [2] 。图 1 展示此设备的总体图以及其操作的基本原理。

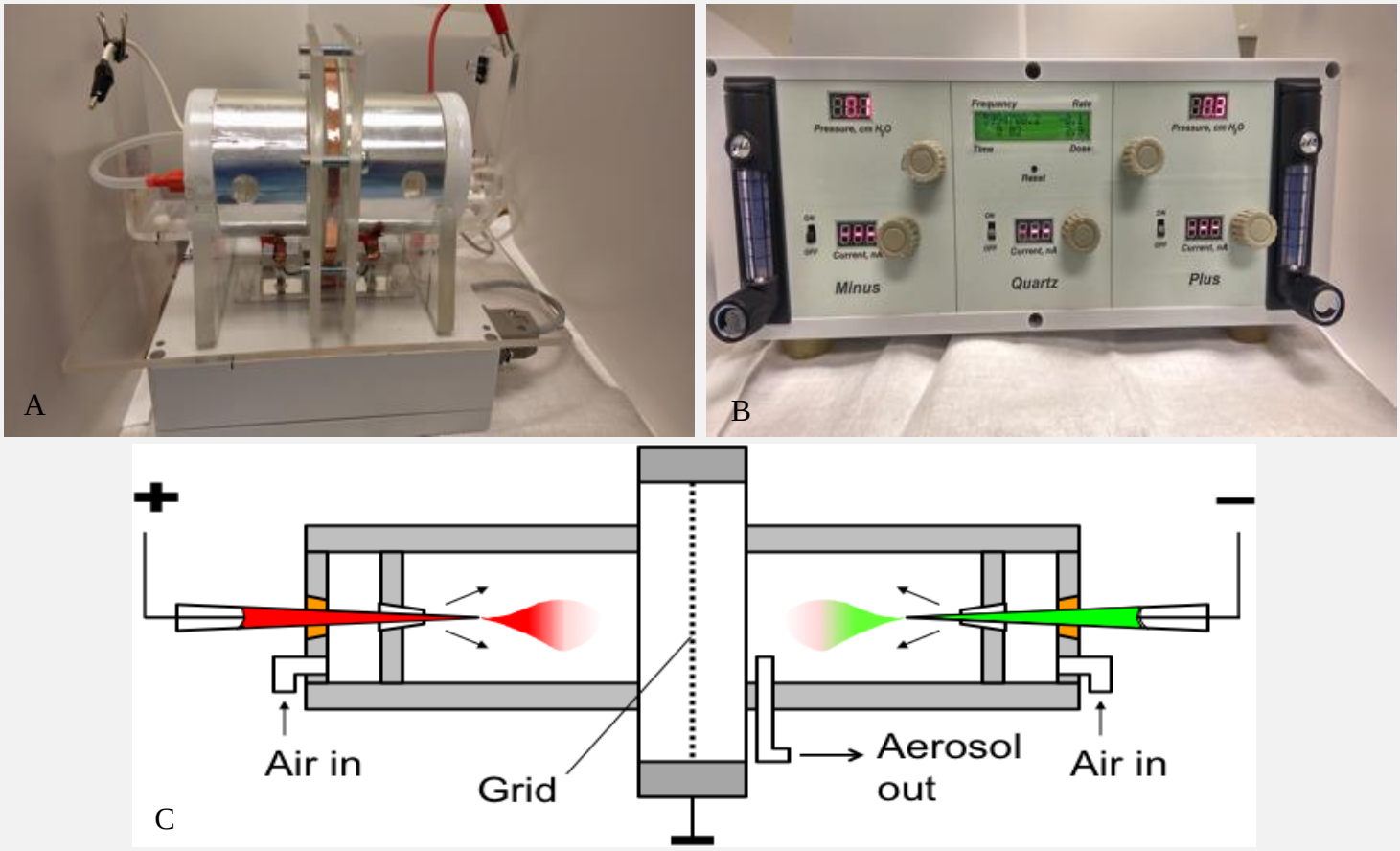

Figure 1. A. General view of nanoaerosol generator unit. B. Control unit. C. Schematic illustrating principle of the generator operation

图 1. A 中的纳米气溶胶发生器单元的总图。 B. 控制单元。 C.. 说明发电机工作原理的示意图。

In a series of experiments a complete retention of the structure and function of enzyme molecules was demonstrated provided atomization was performed at certain environmental and electrical parameters [3,4]. It was estimated that the level of hydrogen peroxide in the nanoaerosol generated is four orders of magnitude below the OSHA permissible exposure limit and does not present any danger upon a long–term inhalation.

在一系列实验中，我们发现：只要把雾化过程控制在适当环境和电气参数条件下,一些酶分子的结构和功能可以完全地保留［3，4］。据估计，在纳米气化溶胶过程中产生的过氧化氢的浓度低于 OSHA 所容许值的上限，故长期吸入无任何危险。

The device prototype has been applied to treat pulmonary tularemia infections in mice. It was found that inhalation of nanoaerosolized levofloxacin resulted in a significant increase in mean time to death, as seen in Fig. 2. The treatment with the same antibiotic encapsulated into nano-

该设备的原型已应用于治疗小鼠肺兔热病感染。我们的实验发现：纳米雾化左氧氟沙星的吸入导致小鼠的平均存活时间显著增长 （如图 2 所示）。将相同的抗生素装入纳米胶囊中用

liposomes before atomization increased survival of the mice to 80% at a total inhaled dose that is approximately 60 fold less than the dose needed to treat mice by oral administration.

于治疗，其可使小鼠的存活率提高百分之八十。以纳米技术治疗所用的药物剂量较口服之剂量低约六十倍。

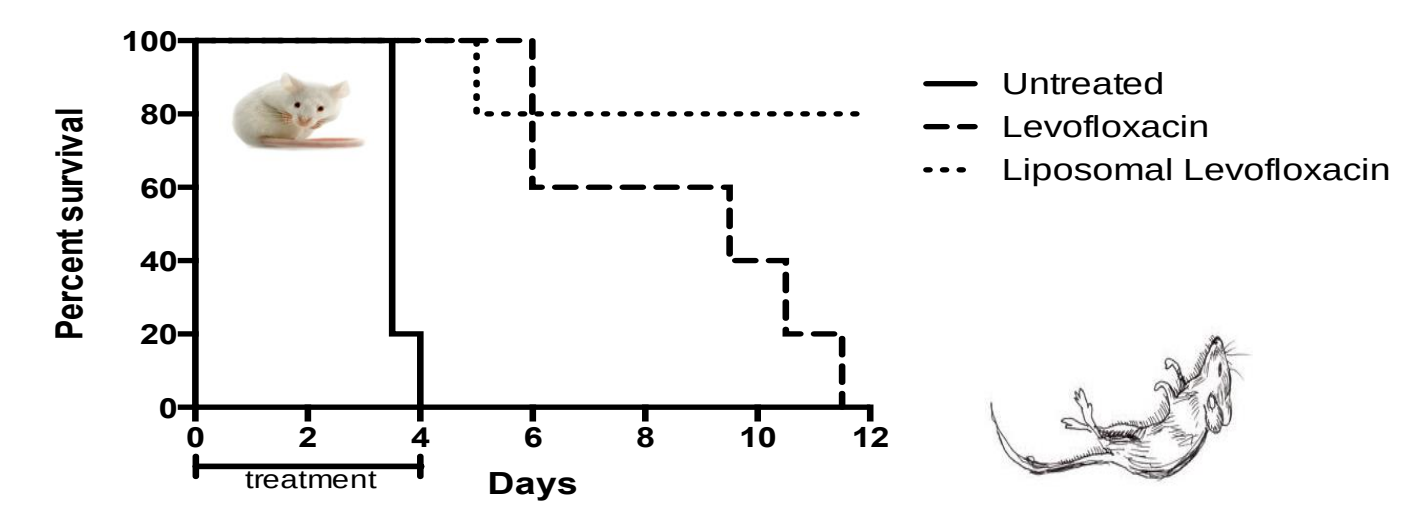

Figure 2. Survival of mice infected with aerosolized *F. novicida*. Mice were treated with nanoaerosolized levofloxacin for 4 hours per day for 5 days (starting at day 0).

图 2. 感染气雾 F. novicida 小鼠的存活。）小鼠用纳米气雾左氧氟沙星治疗，每天 4 小时，共 5 天（第 0 天开始

We also developed nanofilters for collection of biological nanoaerosols into a small volume of buffer for further biochemical or genetic analysis. Nanofilters are manufactured using a modified electrospinning technology [5] in which charged nanofibers are neutralized in air by a cloud of counter-ions in a way similar to that illustrated in figure 1C. It was demonstrated that such filters can be effectively used in collection of biological nanoaerosols, DNA markers of pathogens in clinics and in painless non-invasive collection of probes of lung liquid from exhaled air. A few prototypes have been developed to collect non-volatile biomarkers from exhaled air (see Figure 3).

我们还开发了纳米过滤器，该过滤器可将呼吸系统中的脱落性或者分泌性生物物质收集到小量的缓冲液中，供进一步生化和分子生物学相关的分析。纳米过嚏器是用一种改良的电纺技术制造，在此，激化的纳米纤维被一层反向离子所中和(类似 1C 所示之原理)。我们的实验已显示：以此法制作的纳米纤维可有效地用于临床，收集鼻咽部的分泌或脱落物质，病源体的 DNA 标记， 以及无疼地从呼出的空气中收集肺液。我们已制成几个用于收集非挥发性生物标记物装置的模型(见图 3)。

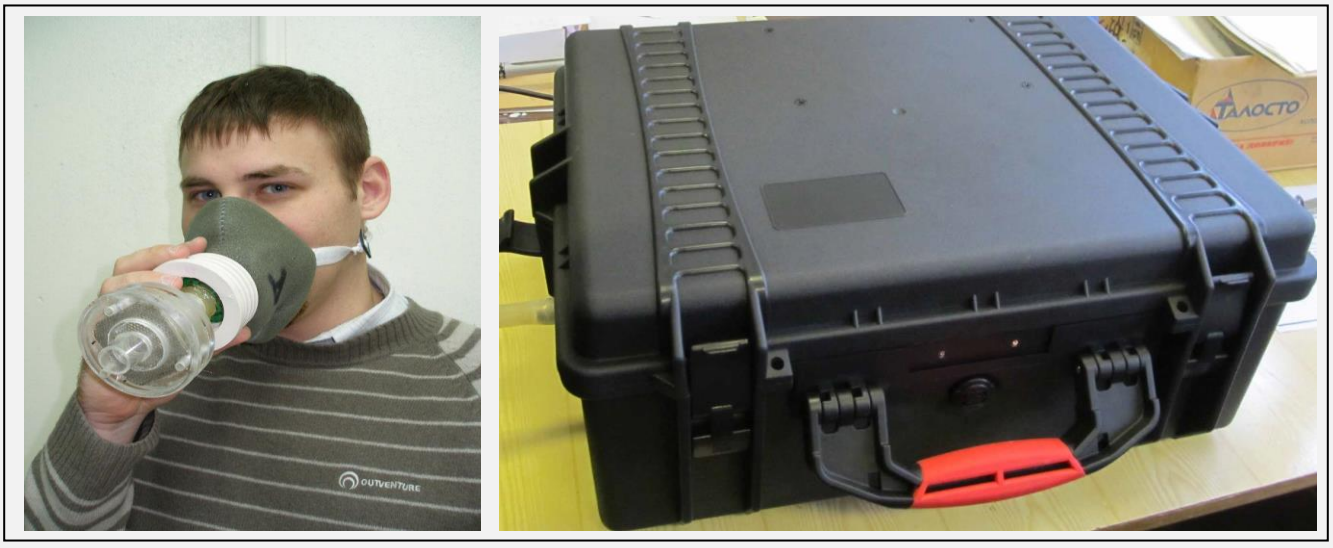

Figure 3. Devices for collection of non-volatile biomarkers from exhaled air.
图 3. 用于从呼吸中收集非挥发性生物标记的装置

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