Advancing Opioid Overdose Intervention: Formulating Novel Spray-Dried Naloxone Microparticles for Pulmonary Delivery

Singh, Anvi (School: Wilsonville High School)

In the last decade, the world has plunged into an opioid epidemic, with overdose deaths surging, amplified by the rise of synthetic drugs. In 2019, opioids accounted for 80% of global drug-related deaths, with overdoses claiming 125,000 lives. Naloxone has been critical in reversing overdoses, primarily administered as the intranasal spray Narcan. However, Narcan has limitations, including 50% nasal bioavailability complemented by a short half-life (60-120 minutes), often requiring repeated doses. Additionally, its rapid opioid reversal can trigger acute withdrawal symptoms. My research developed a novel spray-dried microparticle with a drug-entrapping matrix for efficient and targeted delivery of naloxone. These micron-sized particles reach the deep lungs, enabling rapid systemic uptake via the alveolar-capillary membrane. The preservative-free dry powder system also adds to drug stability and shelf life. The polymers sodium carboxymethyl cellulose and carboxymethyl chitosan were selected to optimize mucoadhesion and facilitate controlled drug release. Microparticles were formulated using a Büchi 290 spray dryer with a naloxone hydrochloride-polymer suspension (20% w/w drug loading) with a yield of 70% w/w. Scanning electron microscopy confirmed an average particle size of 1-5 μm, suitable for deep lung deposition. Drug release was evaluated in phosphate-buffered saline at 1, 5, and 10 minutes via UV-Vis with a 40-320 μg/mL standard curve. High-performance liquid chromatography tandem mass spectrometry estimated entrapment efficiency at 55.55% w/w. These findings suggest that dry-powder pulmonary delivery of naloxone is a viable alternative to Narcan, offering improved bioavailability, stability, and longer action to reduce withdrawal symptoms.

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