NANOPARTICLES FOR BRAIN TARGETING THROUGH NASAL ROUTE: HOPE OR HYPE

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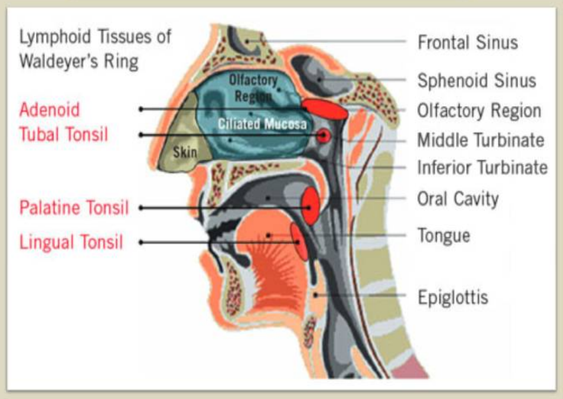
Nasal Physiology



Barriers to Brain Delivery

Physical barrier
(Endothelial cells, Capillary pericytes & Perivascular astrocytes)

Enzymatic barrier
(Various types of ecto-enzymes)

Efflux barrier
(Transporters like p-gp)

Strategies to Overcome Barrier

Invasive Delivery
- Intra-cerebro-ventricular (ICV) infusion
- Intra-thecal delivery
- BBB disruption (Osmotic, Ultrasound, Bradykinin-analogue)
- Lipidization, transporters, Nanocarriers

Non-Invasive Delivery
- Nasal to brain drug delivery

Advantages of Nasal Drug Delivery

- Absence of blood brain barrier
- Rapid onset of action
- Reduce health workers' risks of needle-stick injuries
- Improve patient compliance
- Allow patients to self-medicate
- Can be use chronically

Critical Factors for Nasal Drug Delivery

Physico-chemical factors (Chemical form, Particle Size, Polymorphism etc.)

Formulation factors (pH, Penetration enhancers, Preservatives etc.)

Physiological factors (Pathological condition, blood flow, Clearance etc.)

Patient related factor (Head position, Insertion sight, inhalational speed etc.)

Device related factors (Spray cone angle, turbulence, Injected speed etc.)

Efficiency of Nasal Nanoparticulate Delivery over Nasal and Intravenous Solution

Polymer	Drug	Intranasal Solution	Intravenous route	Reference
Chitosan	Bromocriptine	2 times	3 times	Md et al., 2013
PLGA	Olanzapine	6.35 times	10.86 times	Seju et al., 2011
Chitosan	Venlafaxine	3 times	8 times	Haque et al., 2012
Chitosan	Rivastigmine	2 times	3 times	Fazil et al., 2012
PLA–PEG	Zidovudine	1.3 times	Not Done	Mainardes et al., 2010
Chitosan	Thymoquinone	18 times	More than 100 times	Alam et al., 2012
MPEG-PLA	Nimodipine	1.56 times	Not done	Zhang et al., 2006

Surface Modification of Nanoparticles to Enhance Brain Delivery

Conjugation	Coating
Lectins	Chitosan Coating
Poly Ethylene Glycol	Polysorbate Coating
Wheat germ agglutinin	β- cyclodextrin derivatives

List of Patents for Nasal to Brain Drug Delivery

Inventor	Patent No.	Drug	Description
Francosis et al.	US 6,054,462	Alniditan	•Chitosan nanoparticles •Unit dose nasal spray •Increase bioavailability at brain •Reduce peripheral side effects.
Greco et al.	US 7,989,502 B2	Modafinil	•Lipid Microemulsion •Given through OPTINOSE® •Targeting upper third part of nasal cavity to increase brain delivery.
Frey II	US 6,180,603	Neurologic agaents	•Drug delivered along with lipophillic substance like Phosphatidylserine and ganglioside to increase absorption through olfactory region.

List of Patents for Nasal to Brain Drug Delivery Device

Inventor	Company	Patent No.	Description
Hoekman et al.	Impel Neuropharma INC., WA, US	WO2012119153A2 (2012)	•Propellant based device •Specifically at olfactory region •For both solid and liquid formulations.
Djupesland, P.G.	Optinose AS, Oslo, NO	US 7,347,201 B2 (2008)	•Exhalation breath-actuated device •Comprise of a nosepiece and mouthpiece.
Heinz, H.	Boehringer Ingelheim Pharma GmbH & Co. KG, Germany	EP 2,020,249 A1 (2009)	•Inhaler actuated device •For delivery of powder •Consist of one piercing element, an inhalational channel and an inlet opening at lower housing part.

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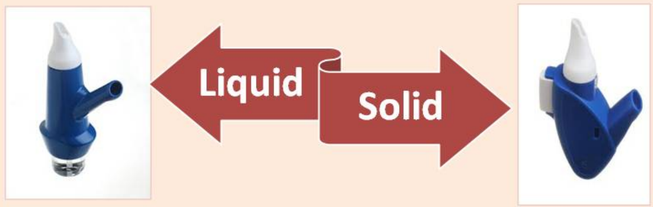
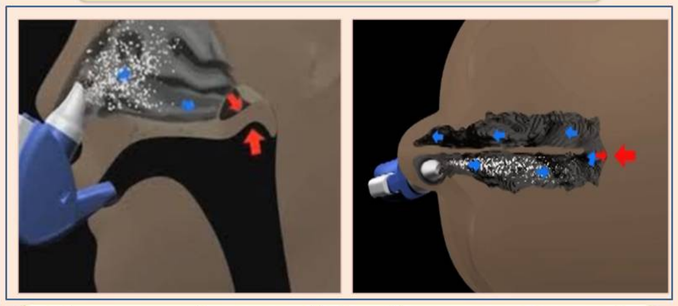
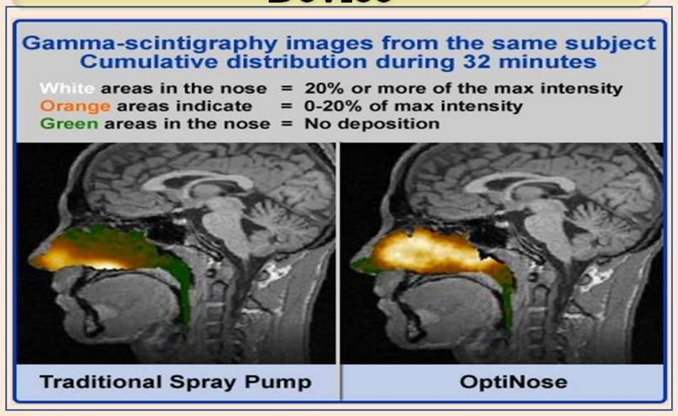


Way to Deliver



Comparison with Conventional Device



Conclusion

- Nanoparticulate formulation improves the efficiency of brain drug delivery via nasal administration as compared to conventional nasal and Intravenous formulation.
- Development of nanoparticulate formulation is a big hope for industrial scientist for treatment of brain diseases. However, delivery by suitable device can only decides its effectiveness.

References

Mistry et al, Nanoparticles for direct nose-to-brain delivery of drugs, International Journal of Pharmaceutics 379 (2009) 146–157

Illum, L. Nasal drug delivery — Recent developments and future prospects. Journal of Controlled Release 161 (2012) 254–263.

http://www.optinose.com , Accessed on 5 Feb. 2013

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