Ramanujam V, et al., J Anesth Clin Care 2020, 7: 046
DOI: 10.24966/ACC-8879/100046

HSOA Journal of Anesthesia and Clinical Care

Short Review

Nanotechnology in Pain Management

Vendhan Ramanujam[1]*, Divya Gunasekaran[2] and Kumaran Ramanujam[3]

[1]*Department of Anesthesia, University of Iowa Hospitals & Clinics, Iowa, USA*

[2]*Department of Electrical and Computer Engineering, University of Massachusetts, Massachusetts, USA*

[3]*Department of Information Technology and Management, Illinois Institute of Technology, Illinois, USA*

Abstract

Pain is the most common reason for people to seek medical care in the United States and it is a significant economic burden. Pharmacotherapy is the first line of approach in its management. Having said so medications do come with a wide range of side effects and abuse or over use potential. This instigates the need to develop effective as well as safe drugs. This is where nanotechnology holds a key and has attracted different industries including the pharmaceuticals. Nanotechnology is conducted at a nanometer scale and can help design drugs at a molecular scale. Designed at that scale, drugs with unique properties such as high bioavailability, receptor specificity, long duration of action and less systemic toxicity have evolved. While nanotechnology-devised smart drugs already exist in the market that can surprise us, many are in the pipeline. As the challenges posed by pain are colossal there is a need for consistent development of safe and effective pain medications, and that can something be accomplished by nanotechnology in our near coming future.

Introducion

Pain management is a known significant challenge in the United States involving nearly 100 million patients and costing at least $560-$635 billion every year. In the efforts to find new, effective and safer modalities to treat pain, a science, engineering, as well a technology conducted at nanoscale has started finding its inroads into the system. Its desirable attribute of designing and developing drugs with targeted delivery has made it a great fit for pharmacological pain management.

The field of medicine is a constant evolution that necessitates exploration of new roads in both diagnostic and therapeutic aspects of this field. One ever-growing interest exists in the research and development of more precise and effective ways in treatment modalities. Pain is the most common reason for people to seek medical care in the United States, with an estimated one-third of its population (100 million people) affected, exceeding diabetes, heart disease, stroke and cancer combined. Being a significant economic burden, costing the society at least $560-$635 billion annually, it is crucial that we continue to strive for newer, effective, and safer modalities to treat pain [1]. This is where we believe nanotechnology holds the future for a more effective drug delivery system to treat pain. The concept of nanotechnology was first propounded by Nobel Laureate Richard Feynman in 1959.

Nanotechnology is defined as science, engineering, and technology conducted at nanoscale. It is the study and application of nanometer technology that can be used across the different realms of science such as: chemistry, biology, physics, material science, engineering, as well as the pharmaceutical industry. The pharmaceutical industry has been showing interest in using nanotechnology to develop highly specific medical intervention, both diagnostic and therapeutic, at the molecular scale (i.e. size below 1000 nm) for curing diseases or repairing damaged tissues, which refers to nanomedicine, a sub-discipline of this technology. It is being used to produce drugs with novel and effective delivery systems that hold much promise. Such drugs can be called as “smart drugs” because by being more specific in targets or delivery, they can be more effective while having decreased systemic side effects and increased safety. The pharmaceutical structure of these novel drugs increases their biocompatibility, further improving safety and reducing adverse effects. Lastly it is their pharmacokinetics, which is much improved to primitive methods that keeps pharmaceutical industries extremely interested. Some of these properties include small size, surface charges, and hydrophobicity that increase absorption, resulting in an overall more bioavailable substance. These nanoparticles can enter human cells via cell-mediated endocytosis; a unique ability achieved by coating particles with hydrophobic polymers, thus avoiding their rapid natural removal entertained by human body. The outer surface of these molecules can be altered with specific proteins or antibodies to aid in binding or interacting with specific tissue, again increasing target selectivity and decreasing systemic effects [2].

With so many desirable attributes of nanotechnology, and pharmacotherapy being the first line of approach in pain management, it makes a good fit in designing effective drugs to treat pain. Currently opioids are the most commonly used drugs. Pain being mostly chronic, patients not responding to basic NSAIDs end up relying on opioids for relief, which is although effective, does not come without a cost. There are a whole slew of side effects included in opioids packages including constipation, drowsiness, and nausea and vomiting; but

***Corresponding author:** Vendhan Ramanujam, Department of Anesthesia, University of Iowa Hospitals & Clinics, Iowa, USA, Tel No: +1 5207045144; E-mail: vcramanuj@gmail.com

Citation: Ramanujam V, Gunasekaran D, Ramanujam K (2020) Nanotechnology in Pain Management. J Anesth Clin Care 7: 046.

Received: January 03, 2020; **Accepted:** January 14, 2020; **Published:** January 21, 2020

there are more than the se that range from urinary retention, postural hypotension, respiratory depression, as well as other CNS related disorders that a majority of patients experience [3]. "Smart drugs" from nanotechnology are targeting specific with high binding capability, higher membrane permeability, longer duration of circulation in blood and action. These features are particularly attractive while treating pain; as such nano drugs can be effectively used for long-term with minimal side effects and decreasing opioids use. They can also be designed to provide a controlled release of substance, which can lead to better patient compliance, reduced oral pill intake, and decreased incidence of abuse of prescription pain medications. These medicines can be controlled via an implantable device that delivers long acting medications, at fixed dose, over a fixed period to maintain constant therapeutic levels, thereby improving efficacy and safety. Lastly, these smart drugs are designed to be highly soluble, thus decreasing bio toxicity. All these features make nanomedicine a likely discipline to pursue to effectively treat pain.

Among the standard drugs used to treat pain, quite a few have been developed using nanotechnology holding the promises of a smart drug. Such analgesics that are FDA approved and marketed are NSADIs such as diclofenac, and opioids such as morphine, fentanyl, and oxycodone. Diclofenac submicron particle capsule has been indicated for mild to moderate acute pain in adults at low doses [4-6]. Data from 4 randomized control trials in patients undergoing surgical procedures approved a single-injection, extended release, epidural morphine sulfate formulation for postoperative pain. The formulation showed better effects when compared to controls receiving either conventional epidural morphine or placebo [7]. An oral, extended release, once-daily formulation containing a mixture of immediate-release and extended-release morphine sulfate for moderate to severe around-the-clock pain without any alternatives was approved following studies that revealed comparable analgesic efficacy and stronger pharmacokinetic profile when compared to controlled release morphine sulfate [8-9]. Nanotechnology designed oral transmucosal fentanyl citrate; fentanyl sublingual tablet and fentanyl nasal spray are being used for breakthrough cancer pain in those who are already receiving and tolerant to opioids therapy following proven results from several clinical trials [10-17]. Pharmacokinetic and pharmacodynamic profile of a newly approved tablet formulation of immediate-release oxycodone for acute and chronic moderate to severe pain is comparable with a regularly developed immediate-release oxycodone [18]. Oromucosal liquid approval for oral pain due to various lesions followed the immediate and clinically significant results that found no difference while comparing CAM2028-control and CAM2028-benzydamine [19]. Furthermore, some nanotechnology designed NSAIDs such as indomethacin, meloxicam, naproxen, celecoxiband ibuprofen are in pipeline at different stages and are expected to be approved and marketed soon [20-23].

With pain being a comorbidity that significantly affects quality of life, inflicting an enormous economic burden both on health system and society, the challenge is colossal. Nanotechnology offers the potential of developing novel and effective drug delivery systems that will effectively treat pain, emphasizing on the beginning of a new era in pain management.

References

1. National Academies Press (2011) Relieving Pain in America: A blueprint for transforming prevention, care, education, and research. National Academies Press, Washington, D.C, USA.
2. Onoue S, Yamada S, Chan HK (2014) Nanodrugs: pharmacokinetics and safety. Int J Nanomedicine 9: 1025-1037.
3. Bagheri SC, Jo C (2008) Clinical Review of Oral and Maxillofacial Surgery. "Opioid Side Effects" Mosby Elsevier Publishers, St. Louis, USA, Page no: 48-52.
4. Manvelian G, Daniels S, Altman R (2012) A phase I study evaluating the pharmacokinetic profile of a novel, proprietary, nano-formulated, lower-dose oral indomethacin. Postgrad Med 124: 197-205.
5. Manvelian G, Daniels S, Gibofsky A (2012) A phase 2 study evaluating the efficacy and safety of a novel, proprietary, nano-formulated, lower dose oral diclofenac. Pain Med 13: 1491-1498.
6. Gibofsky A, Silberstein S, Argoff C, Daniels S, Jensen S, et al. (2013) Lower-dose diclofenac submicron particle capsules provide early and sustained acute patient pain relief in a phase 3 study. Postgrad Med 125: 130-138.
7. Viscusi ER, Martin G, Hartrick CT, Singla N, Manvelian G, et al. (2005) Forty-eight hours of postoperative pain relief after total hip arthroplasty with a novel, extended-release epidural morphine formulation. Anesthesiology. 102: 1014-1022.
8. Caldwell JR, Rapoport RJ, Davis JC, Offenberg HL, Marker HW, et al. (2002) Efficacy and safety of a once-daily morphine formulation in chronic, moderate-to-severe osteoarthritis pain: results from a randomized, placebo-controlled, double-blind trial and an open-label extension trial. J Pain Symptom Manage 23: 278-291.
9. Portenoy RK, Sciberras A, Eliot L, Loewen G, Butler J, et al. (2002) Steady-state pharmacokinetic comparison of a new, extended-release, once-daily morphine formulation, Avinza, and a twice-daily controlled-release morphine formulation in patients with chronic moderate-to-severe pain. J Pain Symptom Manage 23: 292-300.
10. Christie JM, Simmonds M, Patt R, Coluzzi P, Busch MA, et al. (1998) Dose-titration, multicenter study of oral transmucosal fentanyl citrate for the treatment of breakthrough pain in cancer patients using transdermal fentanyl for persistent pain. J Clin Oncol 16: 3238-3245.
11. Portenoy RK, Payne R, Coluzzi P, Raschko JW, Lyss A, et al. (1999) Oral transmucosal fentanyl citrate (OTFC) for the treatment of breakthrough pain in cancer patients: a controlled dose titration study. Pain 79: 303-312.
12. Farrar JT, Cleary J, Rauck R, Busch M, Nordbrock E (1998) Oral transmucosal fentanyl citrate: randomized, double-blinded, placebo-controlled trial for treatment of breakthrough pain in cancer patients. J Natl Cancer Inst 90: 611-616.
13. Lennernäs B, Frank-Lissbrant I, Lennernäs H, Kälkner KM, Derrick R, et al. (2010) Sublingual administration of fentanyl to cancer patients is an effective treatment for breakthrough pain: results from a randomized phase II study. Palliat Med 24: 286-293.
14. Rauck RL, Tark M, Reyes E, Hayes TG, Bartkowiak AJ, et al. (2009) Efficacy and long-term tolerability of sublingual fentanyl orally disintegrating tablet in the treatment of breakthrough cancer pain. Curr Med Res Opin 25: 2877-2885.
15. Lyseng-Williamson KA (2011) Fentanyl pectin nasal spray: in breakthrough pain in opioid-tolerant adults with cancer. CNS Drugs 25: 511-522.
16. Davies A, Sitte T, Elsner F, Reale C, Espinosa J, et al. (2011) Consistency of efficacy, patient acceptability, and nasal tolerability of fentanyl pectin nasal spray compared with immediate-release morphine sulfate in breakthrough cancer pain. J Pain Symptom Manage 41: 358-366.
17. Radbruch L, Torres LM, Ellershaw JE, Gatti A, Luis Lerzo G, et al. (2012) Long-term tolerability, efficacy and acceptability of fentanyl pectin nasal spray for breakthrough cancer pain. Support Care Cancer 20: 565-573.

18. Leibowitz MT, Zamora CA, Brzeczko AW, Stark JG (2014) A single-dose, 3-way crossover pharmacokinetic comparison between immediate-release oxycodone hydrochloride with aversion technology (IRO-A, Oxecta), IRO-a with Niacin, and Oxycodone Hydrochloride (Roxicodone) in healthy adults under fasting conditions. Am J Ther 21: 99-105.

19. Hadjieva T, Cavallin-Ståhl E, Linden M, Tiberg F (2014) Treatment of oral mucositis pain following radiation therapy for head-and-neck cancer using a bioadhesive barrier-forming lipid solution. Support Care Cancer 22: 1557-1562.

20. Altman R, Daniels S, Young CL (2013) Indomethacin submicron particle capsules provide effective pain relief in patients with acute pain: a phase 3 study. Phys Sportsmed 41: 7-15.

21. Young CL, Strand V, Altman R, Daniels S (2013) A phase 2 study of naproxen submicron particle capsules in patients with post-surgical dental pain. Adv Ther 30: 885-896.

22. Dolenc A, Kristl J, Baumgartner S, Planinsek O (2009) Advantages of celecoxib nanosuspension formulation and transformation into tablets. Int J Pharm 376: 204-212.

23. Plakkot S, de Matas M, York P, Saunders M, Sulaiman B (2011) Comminution of ibuprofen to produce nano-particles for rapid dissolution. Int J Pharm 415: 307-314.

Advances In Industrial Biotechnology | ISSN: 2639-5665

Advances In Microbiology Research | ISSN: 2689-694X

Archives Of Surgery And Surgical Education | ISSN: 2689-3126

Archives Of Urology

Archives Of Zoological Studies | ISSN: 2640-7779

Current Trends Medical And Biological Engineering

International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X

Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276

Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292

Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370

Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594

Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X

Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562

Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608

Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879

Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397

Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751

Journal Of Aquaculture & Fisheries | ISSN: 2576-5523

Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780

Journal Of Biotech Research & Biochemistry

Journal Of Brain & Neuroscience Research

Journal Of Cancer Biology & Treatment | ISSN: 2470-7546

Journal Of Cardiology Study & Research | ISSN: 2640-768X

Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943

Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771

Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844

Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801

Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978

Journal Of Cytology & Tissue Biology | ISSN: 2378-9107

Journal Of Dairy Research & Technology | ISSN: 2688-9315

Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783

Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X

Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798

Journal Of Environmental Science Current Research | ISSN: 2643-5020

Journal Of Food Science & Nutrition | ISSN: 2470-1076

Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X

Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566

Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485

Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662

Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999

Journal Of Hospice & Palliative Medical Care

Journal Of Human Endocrinology | ISSN: 2572-9640

Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654

Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493

Journal Of Light & Laser Current Trends

Journal Of Medicine Study & Research | ISSN: 2639-5657

Journal Of Modern Chemical Sciences

Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044

Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X

Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313

Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400

Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419

Journal Of Obesity & Weight Loss | ISSN: 2473-7372

Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887

Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052

Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X

Journal Of Pathology Clinical & Medical Research

Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649

Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670

Journal Of Plant Science Current Research | ISSN: 2639-3743

Journal Of Practical & Professional Nursing | ISSN: 2639-5681

Journal Of Protein Research & Bioinformatics

Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150

Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177

Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574

Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060

Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284

Journal Of Toxicology Current Research | ISSN: 2639-3735

Journal Of Translational Science And Research

Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193

Journal Of Virology & Antivirals

Sports Medicine And Injury Care Journal | ISSN: 2689-8829

Trends In Anatomy & Physiology | ISSN: 2640-7752