International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

International Journal of Pharmacology 8 (7): 657-658, 2012
ISSN 1811-7775 / DOI: 10.3923/ijp.2012.657.658

Does Mambalgins Obtained from Black Mamba Venom have Solution for Morphine Related Side-Effects?

Muhammad Nouman Sohail
Asian Network for Scientific Information, Faisalabad, Pakistan

During last decade, improvements in medical sciences and adaptation of latest technology have changed the trend of medical practices and significant increase in number of performed surgeries is one of these changing trends. After surgery due to tissue trauma or direct nerve injury, patients suffer with severe pain; different analgesics are used to overcome this postoperative pain. Mind receives pain signals from affected body part via various pathways and all of the commonly used analgesics mainly target different components of these pathways (Vane and Botting, 1995; Graham and Scott, 2005). If postoperative pain is not managed properly then it may lead to deep vein thrombosis, pulmonary embolism, coronary ischemia, myocardial infarction, pneumonia and many other related complications. Morphine is among the group of most commonly administrated medicines for the treatment of postoperative pain. Despite its excellent pain relief activity the use of morphine cause serious side effects, such as urinary retention, pruritus and postoperative nausea and vomiting (Cousins and Mather, 1984). Moreover morphine also causes respiratory depression, constipation, sexual dysfunction, seizure (convulsions), hyperalgesia, fluid retention, change of mental status and edema (Ruan, 2007).

Acid-Sensing Ion Channels (ASICs) are an important class of pH detecting receptors that cause pain when activated in animal and human tissues. Currently there are four genes (ASIC1, ASIC2, ASIC3 and ASIC4) that code for five different protein of ASIC family, which are believed to be the potential target for pain and CNS diseases (Sluka *et al*., 2009). Recently Diochot *et al.* (2012) conducted a study in which they identified three-finger peptide form black mamba venom, which showed potential analgesic effect by effectively blocking the Acid-sensing ion channels (ASICs) in peripheral, pain-sensing nerves and central pain pathways. They named the newly identified protein as "mambalgins" and its tow identified polypeptides as "mambalgin-1" and "mambalgin-2". The analgesic effect of mambalgins was found to be as effective as that of morphine but with no side-effects, when administrated in mice. This newly discovered peptide has unique property that it can block both homomeric (ASIC1a) and heteromeric (ASIC1a = ASIC2a or ASIC1a = ASIC2b) channels, which represents all of the ASIC channel subtypes expressed in the central nervous system. Moreover mambalgins were resistant to naloxone, which means that it does not utilize the opiates pathway; hence does not cause any opiate related side-effects (e.g. addiction and respiratory distress). They concluded that observed analgesic effect of mambalgins is because it targets nociceptors and central neurons but through different ASIC subtypes; moreover, ASICb plays an important role in nociception and inflammatory hyperalgesia.

Morphine is being used either alone or in combination with other drugs for the treatment of pain especially in post operative pain but its related side effects urged the scientist to find the alternatives of this drug having same level of analgesic effects but with no or less side effects. Identification of drug targets which can reduce the pain but do not cause any side-effects is an ideal approach; as Hayes and Tyers (1983) showed that those opiates which exert their analgesic effect by targeting the μ receptors also cause opiate related side effect by interacting with same receptors. The two newly discovered polypeptides by Diochot *et al.* (2012) showed analgesic effect as strong as of morphine but without morphine related side-effects and have potential to serve as the promising analgesic in future. But still there is a long way to go because researchers have characterized these peptides in mouse model and more research is required to determine their safety for human use.

REFERENCES

Cousins, M.J. and L.E. Mather, 1984. Intrathecal and epidural administration of opioids. Anaesthesiology, 61: 276-310.

Diochot, S., A. Baron, M. Salinas, D. Douguet and S. Scarzello *et al.*, 2012. Black mamba venom peptides target acid-sensing ion channels to abolish pain. Nature. 10.1038/nature11494.

Graham, G.G. and K.F. Scott, 2005. Mechanism of action of paracetamol. Am. J. Therapeutics, 12: 46-55.

Hayes, A.G. and M.B. Tyers, 1983. Determination of receptors that mediate opiate side effects in the mouse. Br. J. Pharmacol., 79: 731-736.

Ruan, X., 2007. Drug-related side effects of long-term intrathecal morphine therapy. Pain Physician, 10: 357-365.

Sluka, K.A., O.C. Winter and J.A. Wemmie, 2009. Acid-sensing ion channels: A new target for pain and CNS diseases. Curr. Opin. Drug Discovery Dev., 12: 693-704.

Vane, J.R. and R.M. Botting, 1995. New insights into the mode of action of anti-inflammatory drugs. Inflamm. Res., 44: 1-10.