Development of Sustained Release Oxycodone Hydrochloride Tablets Using Modulating Release Barrier

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Introduction

Oxycodone is a semisynthetic opioid agonist that provides effective relief for moderate to severe pain in cancer[1,2] and postoperative patients.[3] The pharmacokinetic and steady state pharmaco-dynamic studies with immediate release (IR) oxycodone have shown it to be well tolerated, with adverse effects similar to those of other opioids.[1,2,4,5] Oxycodone oral bioavailability in humans is 60 % (range 50-87 %)[2,4,5] The terminal elimination half-life is independent of dose, with modest inter-individual differences. Controlled release (CR) morphine has been the drug of choice in chronic cancer pain, being a more convenient treatment regimen than IR morphine.[6] Recently, a CR formulation of oxycodone was introduced.

Objectives

Sustained release oral oxycodone systems offer the clinical advantage of less frequent dosing with an increase in quality of life for patients with chronic pain requiring repeated-dose opioid analgesia. So, the first objective of this study was to develop an oral sustained release oxycodone tablet using modulating release barrier. The second objective of this study was to determine the capability of the designed system and to provide the same in vitro release profile, using the same formulation containing several doses of oxycodone.

Methods

Hydroxypropylmethylcellulose (HPMC) were major polymeric constituents of the delivery system. Oxycodone hydrochloride were used as hydrophilic model drug. The double layered tablet was produced by compressing particulate systems on single-punch hydraulic laboratory press with a 9.5-mm diameter punch and die. Drug release tests were conducted according to USP 27 Apparatus 2 guidelines. (paddle method) Samples were withdrawn at predetermined time intervals and analyzed for drug content using an HPLC systems at a wavelength of 230nm.

Mixing (v-mixer)

↓

Screening (30mesh, Oscilator)

↓

Post-mixing (Lubricant, v-mixer)

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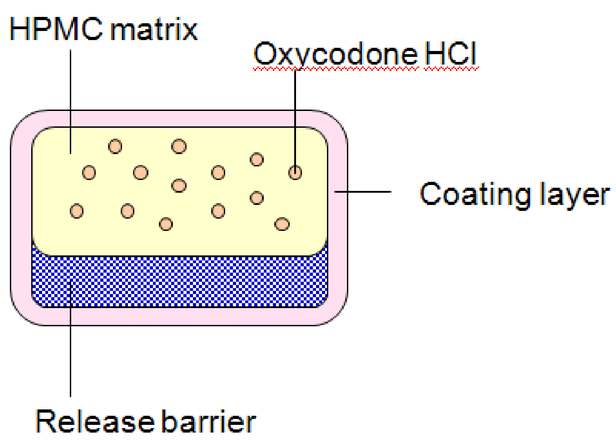
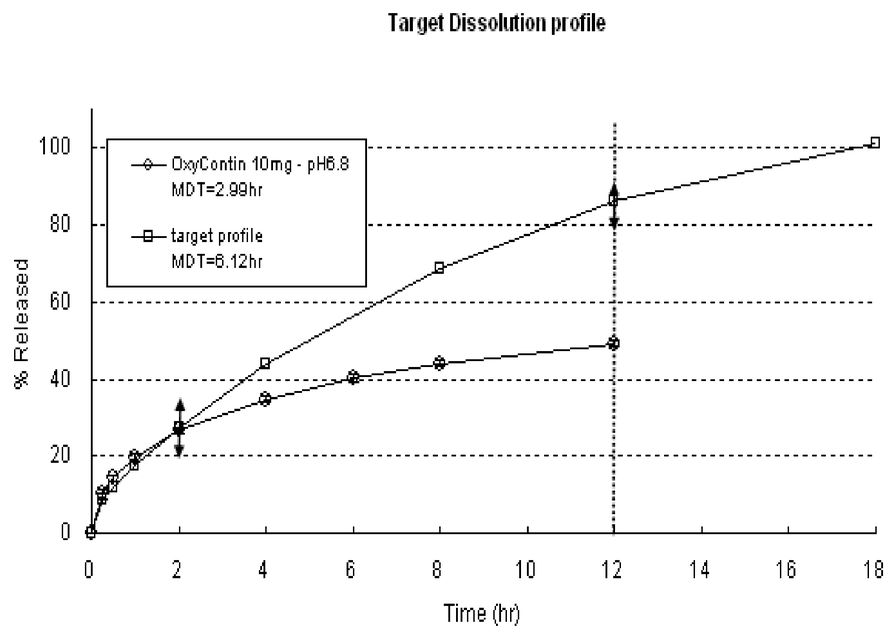
Tableting (Rotary tableting M/C)

Results

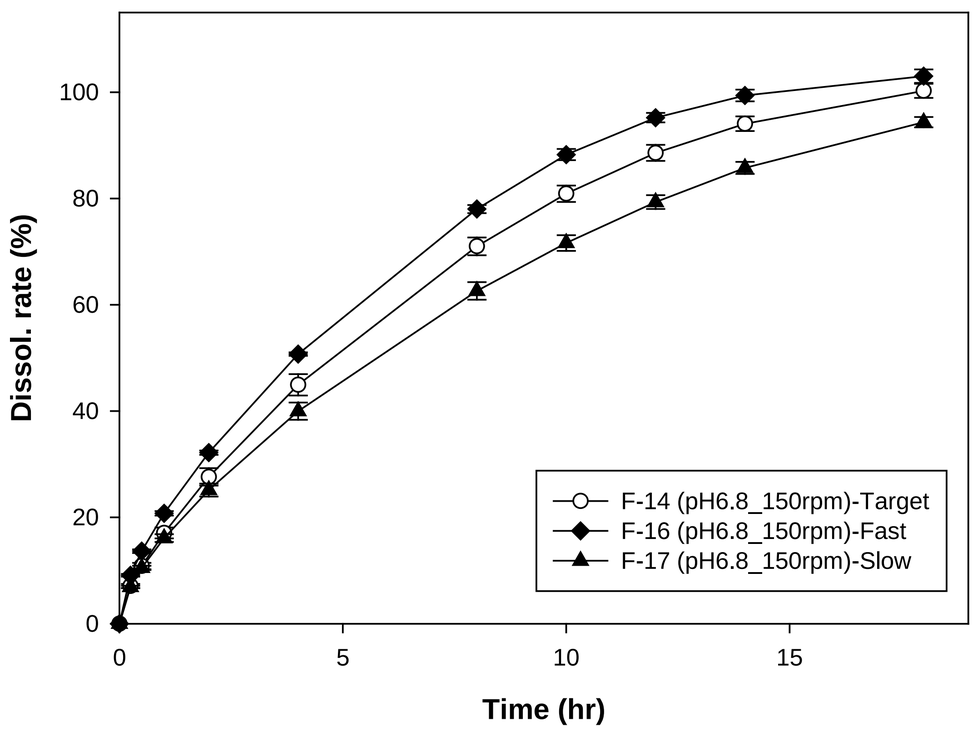
Concept and target profile of double-layered tablets

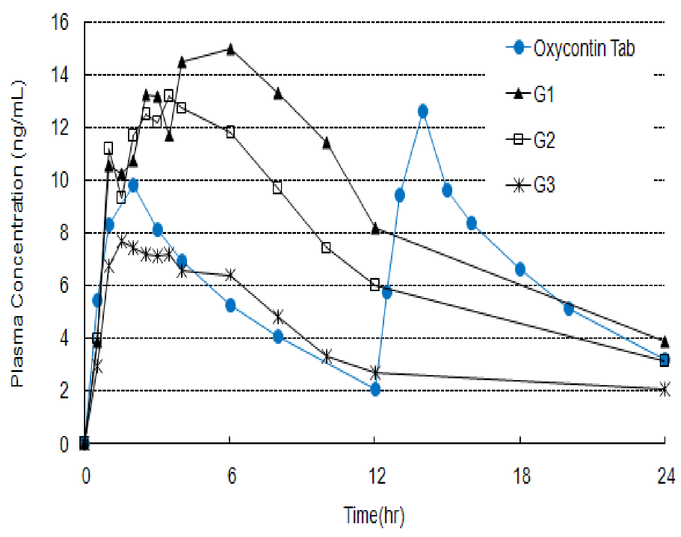


$$\text{MDT(mean dissolution time)} = \frac{\sum^{i} t_i \times \Delta M_i}{M_0}$$



Dissolution and animal PK profile





- Using the information of matrix tablets, a double layered tablet with release barrier was designed and evaluated to overcome the limitations of the matrix tablet and to develop sustained release formulations.
- The double layered tablets showed more consistent release kinetics than the matrix tablets.

	$AUC_{0\sim24}$	C_{max}	T_{max}	$t_{1/2}$
Oxycontin®CR	158.16±105.51	12.62±7.66	1.50±0.55	3.29
G1 (Target)	268.07±147.01	18.06±10.46	4.08±2.48	9.56
G2 (Fast)	237.07±180.08	16.66±10.75	3.25±3.49	11.78
G3 (Slow)	157.20±125.80	9.26±2.56	3.25±2.30	18.82

Conclusions

- A novel double layered tablet consisting of a water-soluble matrix and barrier layer was investigated to develop a preferable once-a-day formulation containing oxycodone hydrochloride as a hydrophilic model drug.
- These findings can give good information for the development of sustained drug delivery systems, especially once-a-day administration.

*** Reference**

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