Intelligent drug delivery system
(Figure 1: Intelligent drug delivery system)
Fig. 1: Diseases known to display circadian rhythm
Table 1. Diseases required pulsatile delivery

<table>
<thead>
<tr>
<th>Chronological behavior</th>
<th>Drugs used</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid secretion is high in the afternoon and at night</td>
<td>H2 blockers</td>
<td>Peptic ulcer</td>
</tr>
<tr>
<td>Precipitation of attacks during night or at early morning</td>
<td>β2 agonist, Antihistamines</td>
<td>Asthma</td>
</tr>
<tr>
<td>BP is at its lowest during the sleep cycle and rises steeply during the early morning</td>
<td>Nitroglycerin, calcium channel blocker, ACE inhibitors</td>
<td>Cardiovascular diseases</td>
</tr>
<tr>
<td>Pain in the morning and more pain at night</td>
<td>NSAIDs, Glucocorticoids</td>
<td>Arthritis</td>
</tr>
<tr>
<td>Increase in the blood sugar level after meal</td>
<td>Sulfonylurea, Insulin</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Cholesterol synthesis is generally higher during night than day time</td>
<td>HMG CoA reductase inhibitors</td>
<td>Hypercholesterolemia</td>
</tr>
</tbody>
</table>
Classification of intelligent drug delivery system

Intelligent Delivery System

- System Utilizing Enzymes
  - Urea Responsive
  - Glucose Responsive
  - Morphine Triggered
- System Utilizing Chelation
- System Utilizing Antibodies
- Responsive System
  - pH Sensitive
  - Thermosensitive
  - Inflammation Responsive
  - Glucose and Other Saccharide Sensitive
- Pulsatile System
  - Electrically Modulated
  - Photoresponsive
  - Magnetically Modulated
METHODS FOR PULSATILE DRUG DELIVERY
ENTERIC COATED PULSINCAP
ORAL ADMINISTRATION

\[ \text{Drug formulation} \rightarrow \text{Water soluble cap} \rightarrow \text{Acid insoluble film coat} \rightarrow \text{Hydrogel plug} \rightarrow \text{Water insoluble body} \]

STOMACH EMPTYING

\[ \text{Cap dissolves in intestinal juice} \rightarrow \text{Hydrogel plug expands} \]

INTESTINAL FLUID

\[ \text{Drug released in colon} \rightarrow \text{Swollen ejected plug} \]

Figure 3:
Different stages in drug release from Pulsincap.
Fig. 8 The Pulsincap® system. (From Ref. [51].)
Fig 4: Plan of Port® System

- Immediate release
- Plug
- Osmotic charge, Programmed release
- Semipermeable membrane
  Coated gelatin capsule
Drug Release Mechanism From PORT System

Step 1
Cap dissolves off
IR or MR dose is released

Step 2
Energy source is activated by
controlled permeation of GI fluid

Step 3
Time-released plug is expelled

Step 4
Pulse or sustained release of 2nd dose

Fig 5: Drug release mechanism from PORT system
b. ‘TIME CLOCK’ System:

Fig.11: ‘TIME CLOCK’ System (VIPUL P. PATEL n.d.)
**Fig. 6:** Schematic diagram of Delivery systems with erodible coating layer.

**Fig. 7:** Schematic diagram of Delivery systems with rupturable coating layer.
<table>
<thead>
<tr>
<th>Technology</th>
<th>Mechanism</th>
<th>Proprietary name and dosage form</th>
<th>API</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>OROS*</td>
<td>Osmotic mechanism</td>
<td>Covera-H5*; XL tablet</td>
<td>Verapamil HCL</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Three dimentional printing*</td>
<td>Externally regulated system</td>
<td>Their Form*</td>
<td>Diclofenac sodium</td>
<td>Inflammation</td>
</tr>
<tr>
<td>DIFFUCAPS*</td>
<td>Multiparticulate system</td>
<td>Innopran*; XL tablets</td>
<td>Verapamil HCL, propranolol HCL</td>
<td>Hypertension</td>
</tr>
<tr>
<td>PulsincapTM</td>
<td>Rupturable system</td>
<td>PulsincapTM</td>
<td>Dofetilide</td>
<td>Hypertension</td>
</tr>
</tbody>
</table>
Fig. 4 Responsive polymer-based hormone release. Release mechanism of P(MAA-g-EG) pH-responsive hydrogel system coupled with glucose oxidase (GOD) for controlled insulin release depending on glucose concentration (modified according to De la Heras Alarcón et al. 2004).
SYSTEMS UTILIZING ENZYMES
Fig. 2. Enzymatic pathway for conversion of glucose to hydrogen peroxide and electrons.
naltrexone dispersed in biodegradable polymer

Morphine-lipase conjugate complexed with antibody

(Figure 5: Morphine triggered naltrexone delivery)