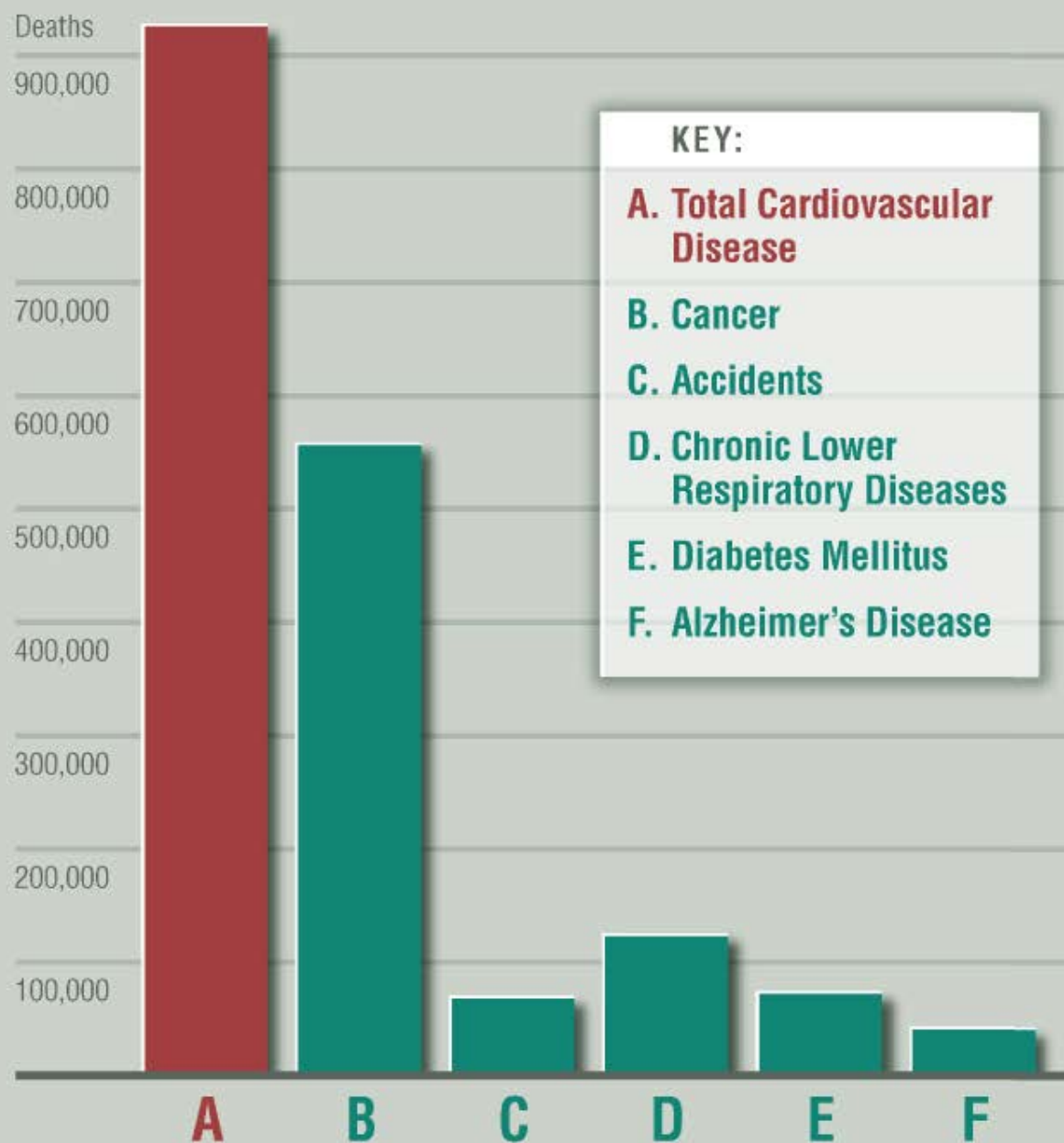


Leading Causes of Death in the United States 2002



Source: CDC/NCHS

Economic Cost of Cardiovascular Disease in the United States – 2005



Estimated Direct Costs:
\$241.9 Billion

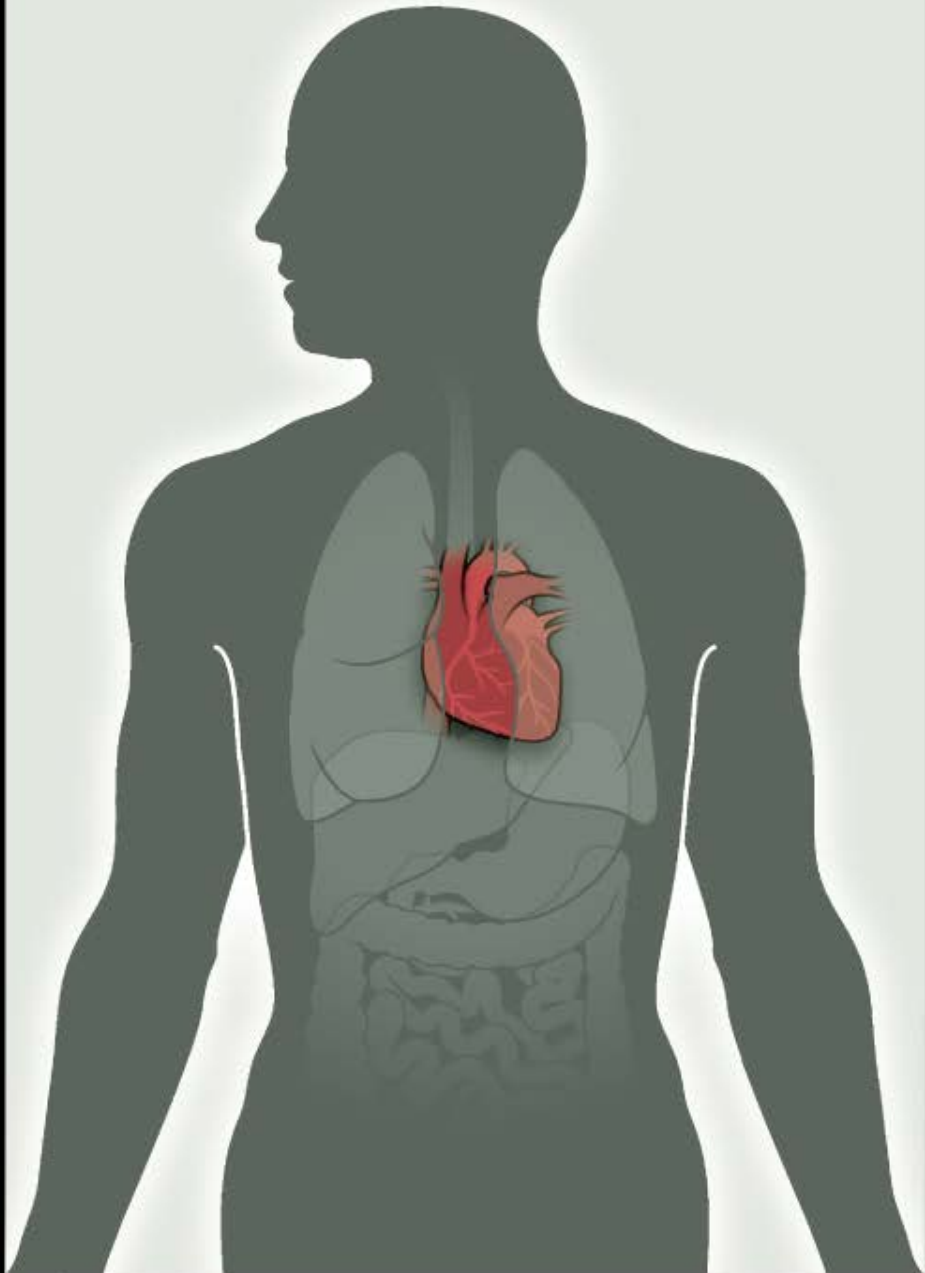
Estimated Indirect Costs:
\$151.6 Billion

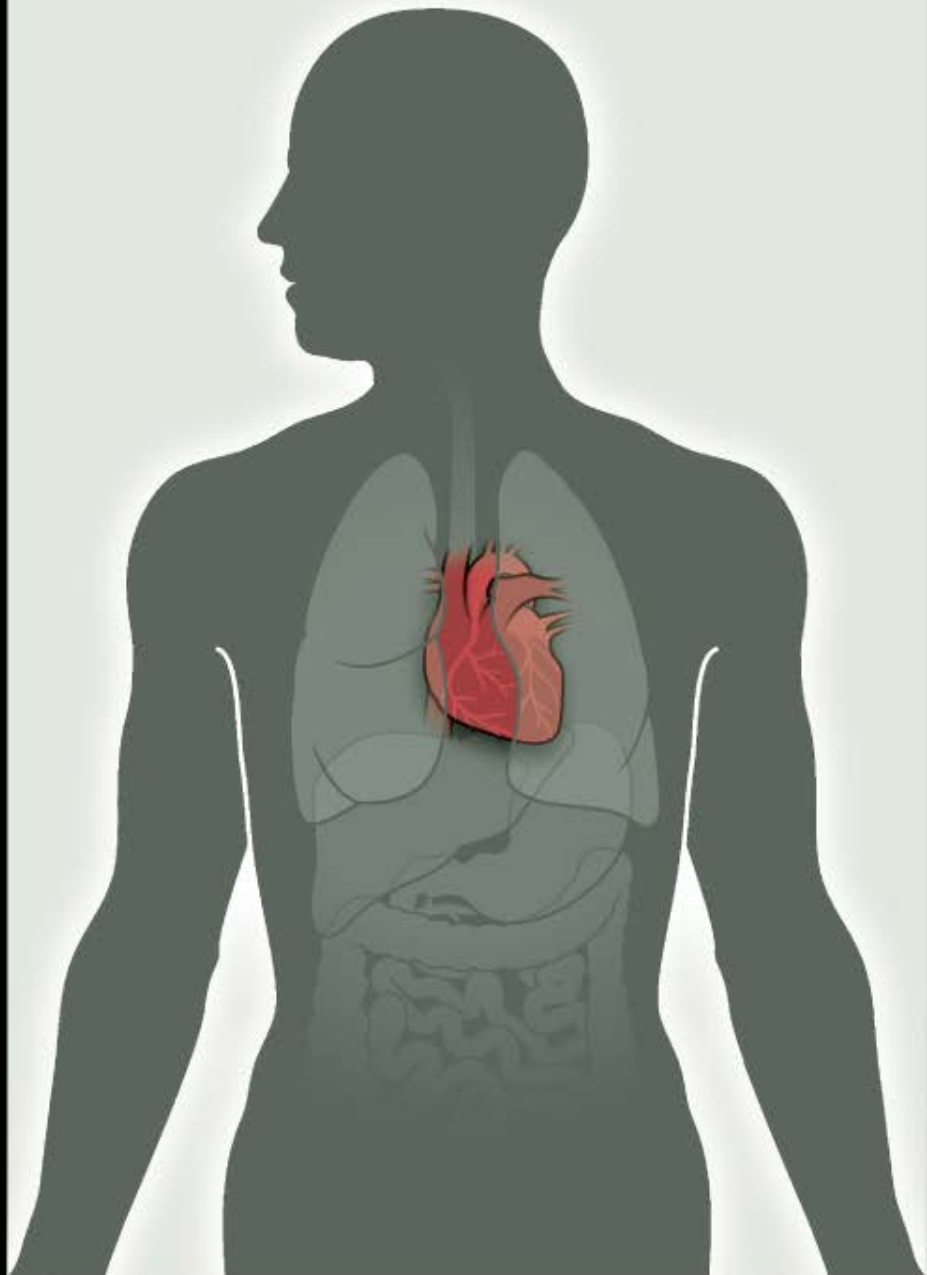
LOSS OF PRODUCTIVITY, DISABILITY AND DEATH

Source: Heart Disease and Stroke Statistics — 2005 Update, American Heart Association, pg. 53

Some Types of Cardiovascular Disease:

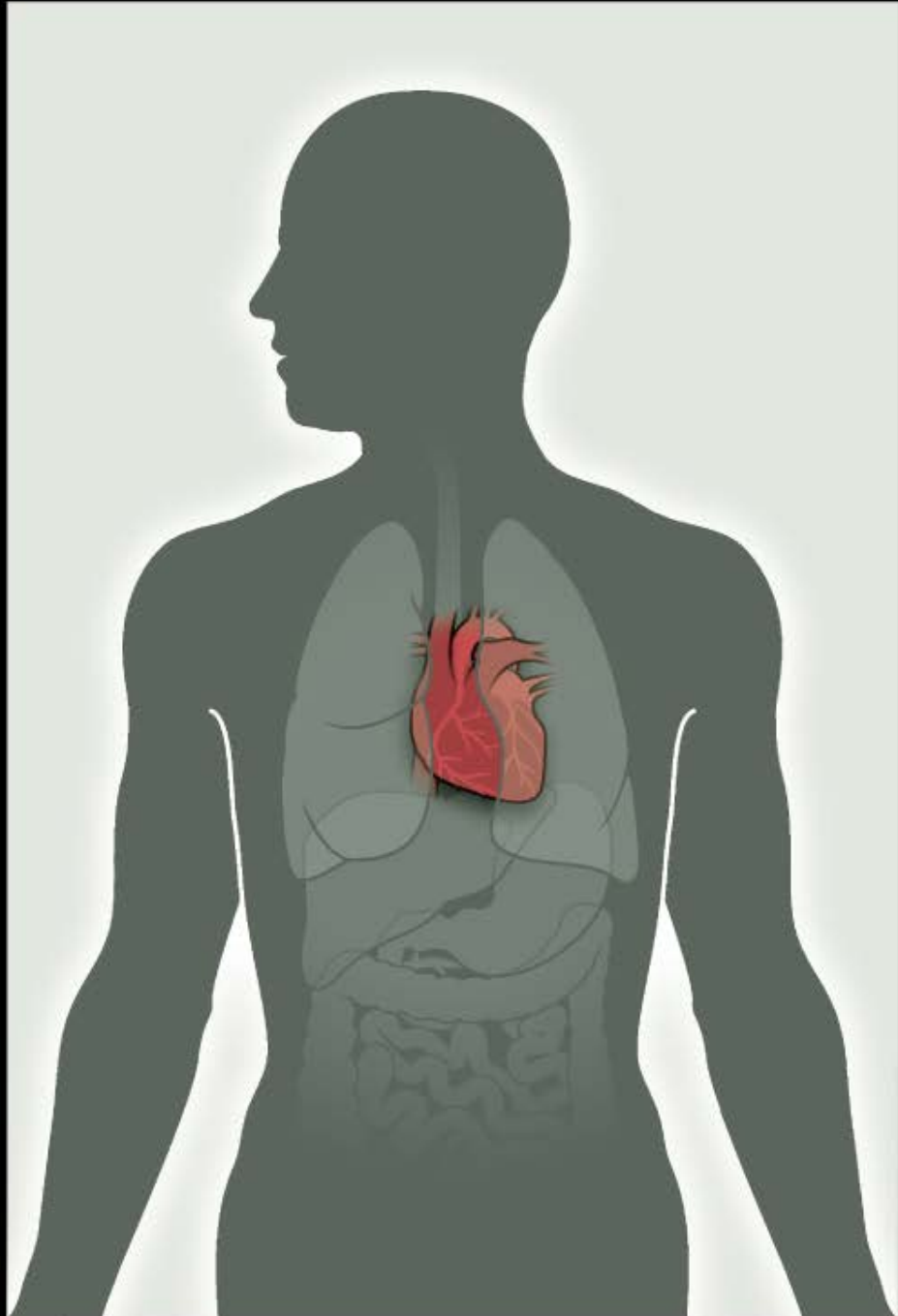
- **Angina Pectoris**





Some Types of Cardiovascular Disease:

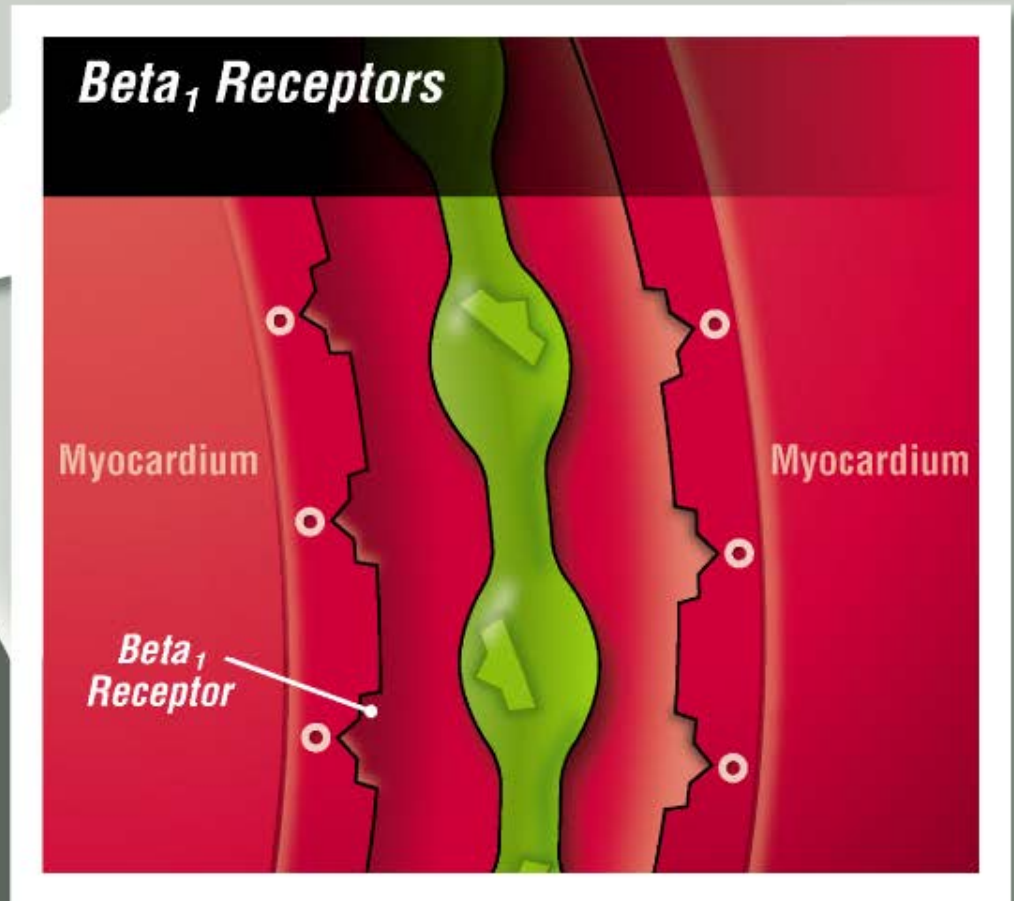
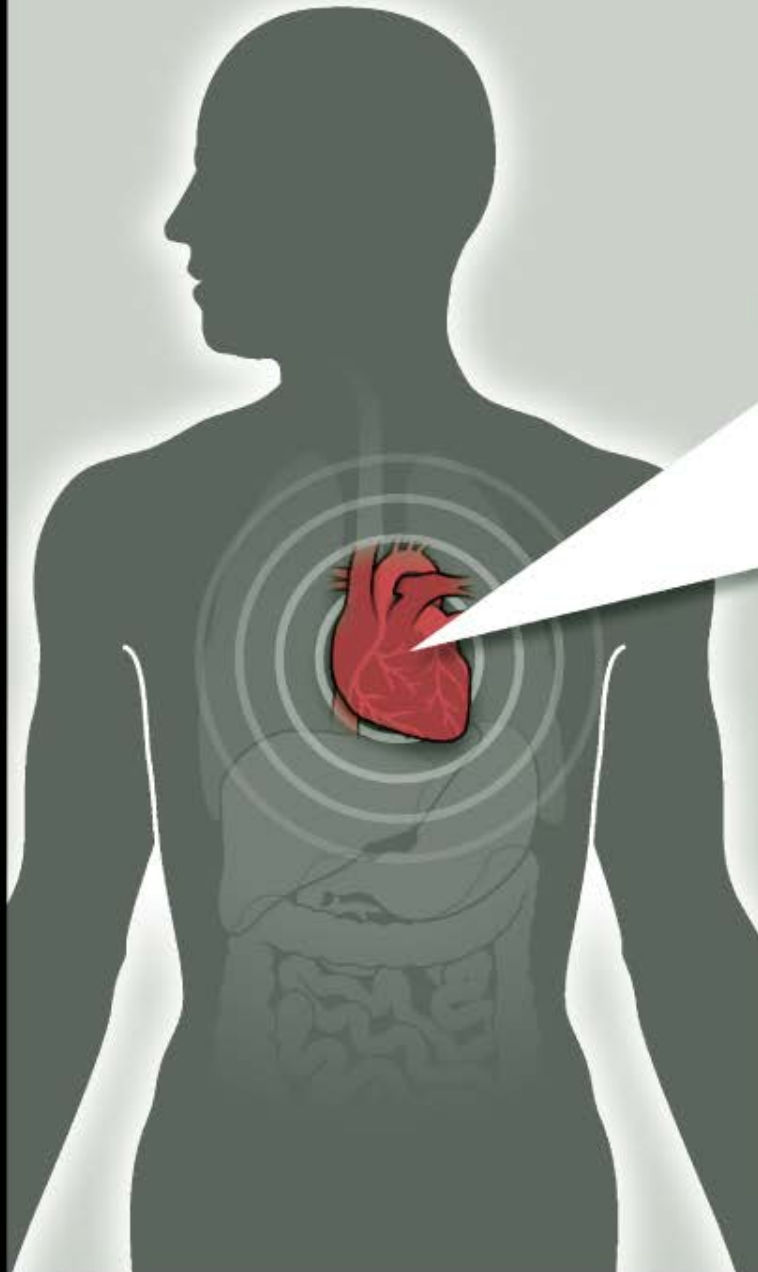
- Angina Pectoris
- Hypertension



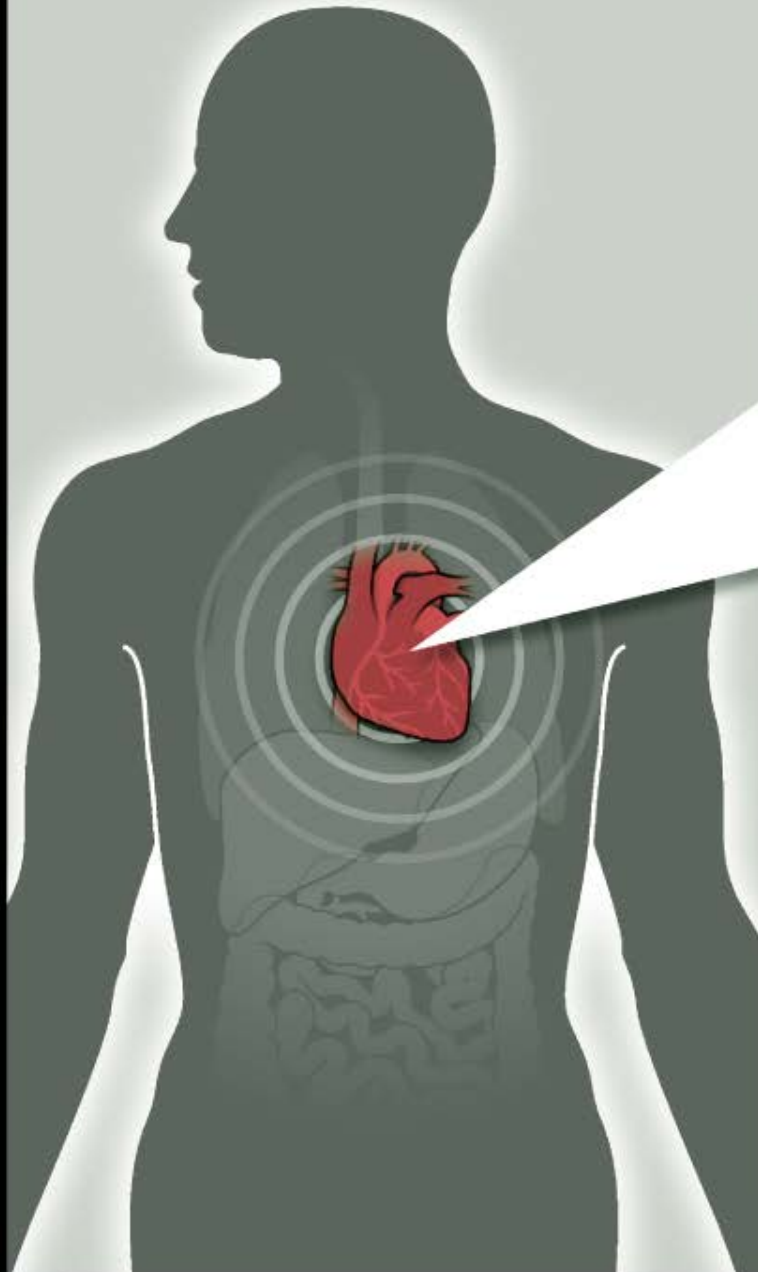
Some Types of Cardiovascular Disease:

- Angina Pectoris
- Hypertension
- **Heart failure**

Beta₁ Adrenergic Receptors in the Heart



Beta₁ Adrenergic Receptors in the Heart

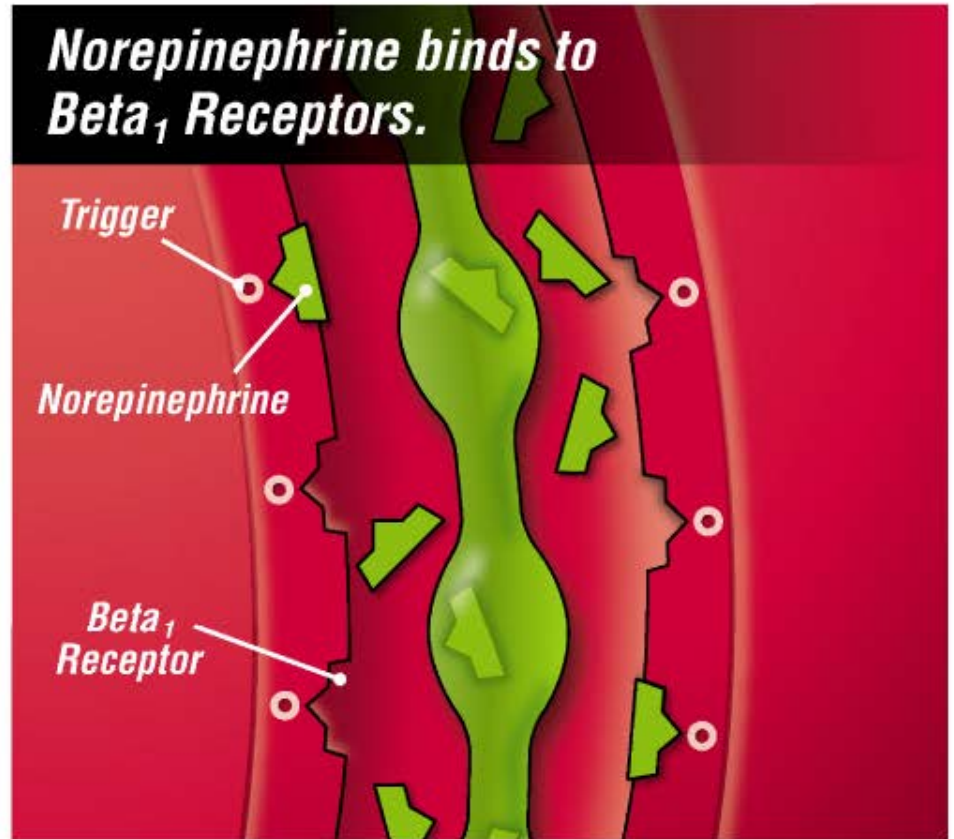


***Norepinephrine binds to
Beta₁ Receptors.***

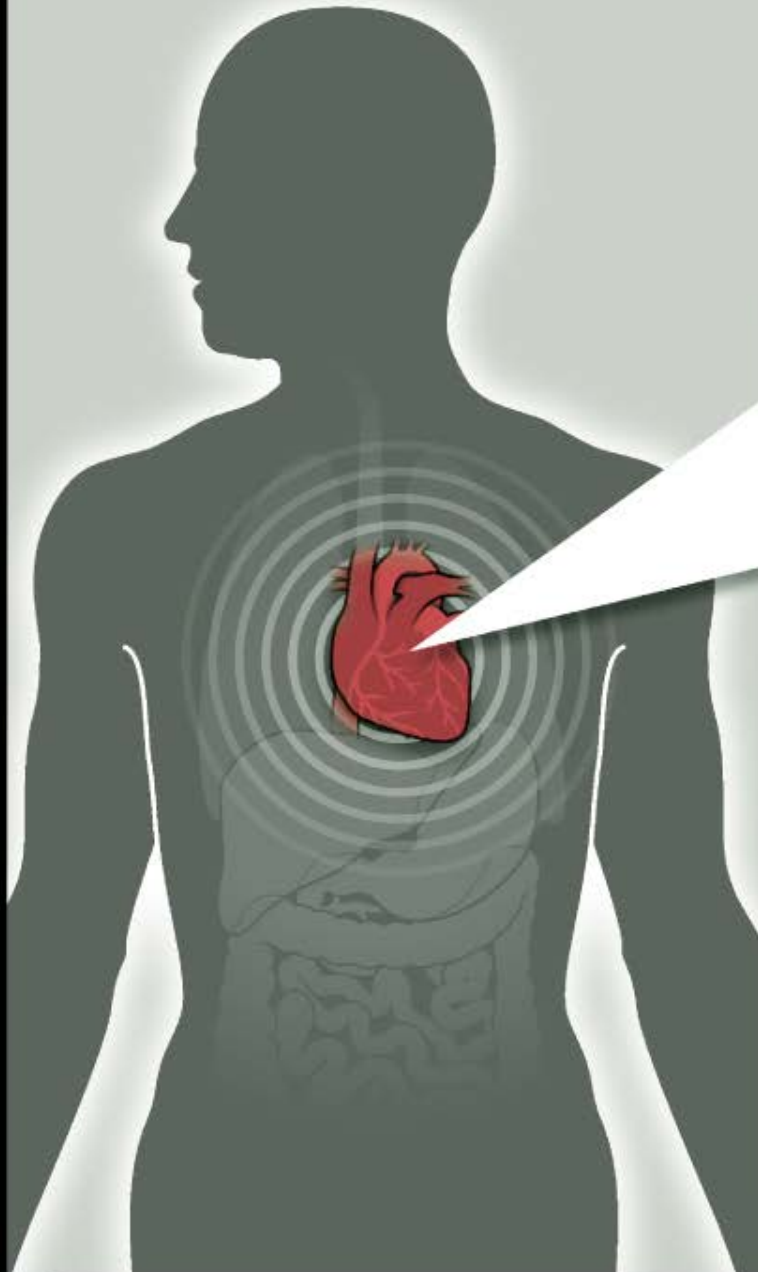
Trigger

Norepinephrine

*Beta₁
Receptor*



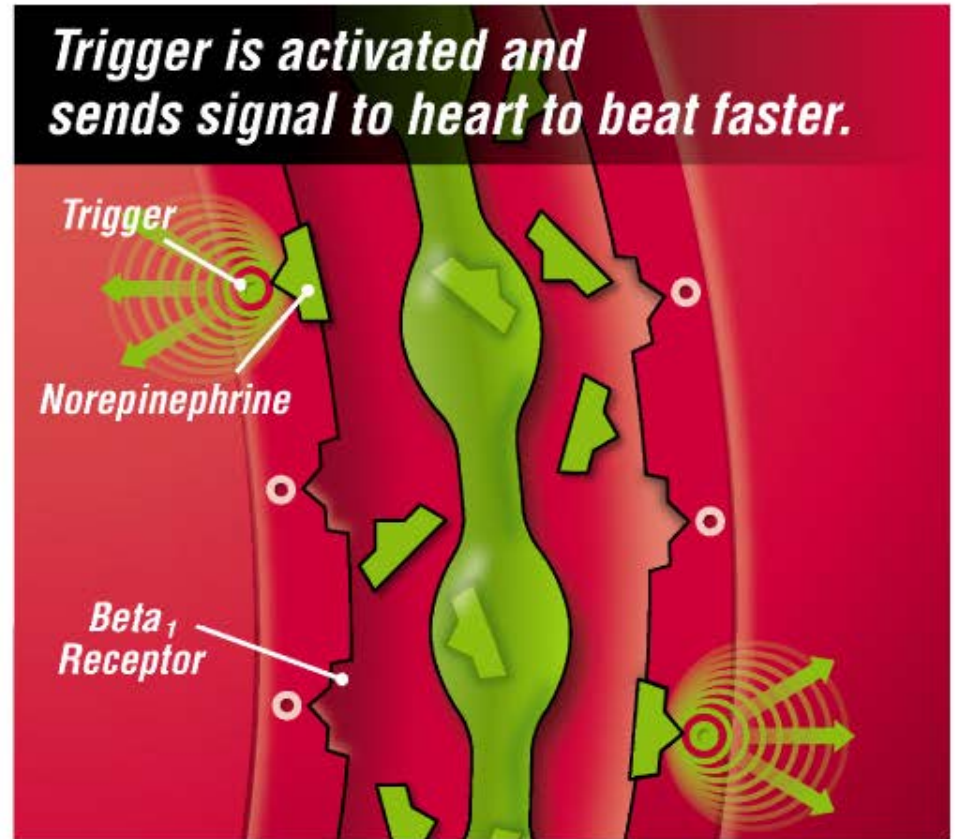
Beta₁ Adrenergic Receptors in the Heart



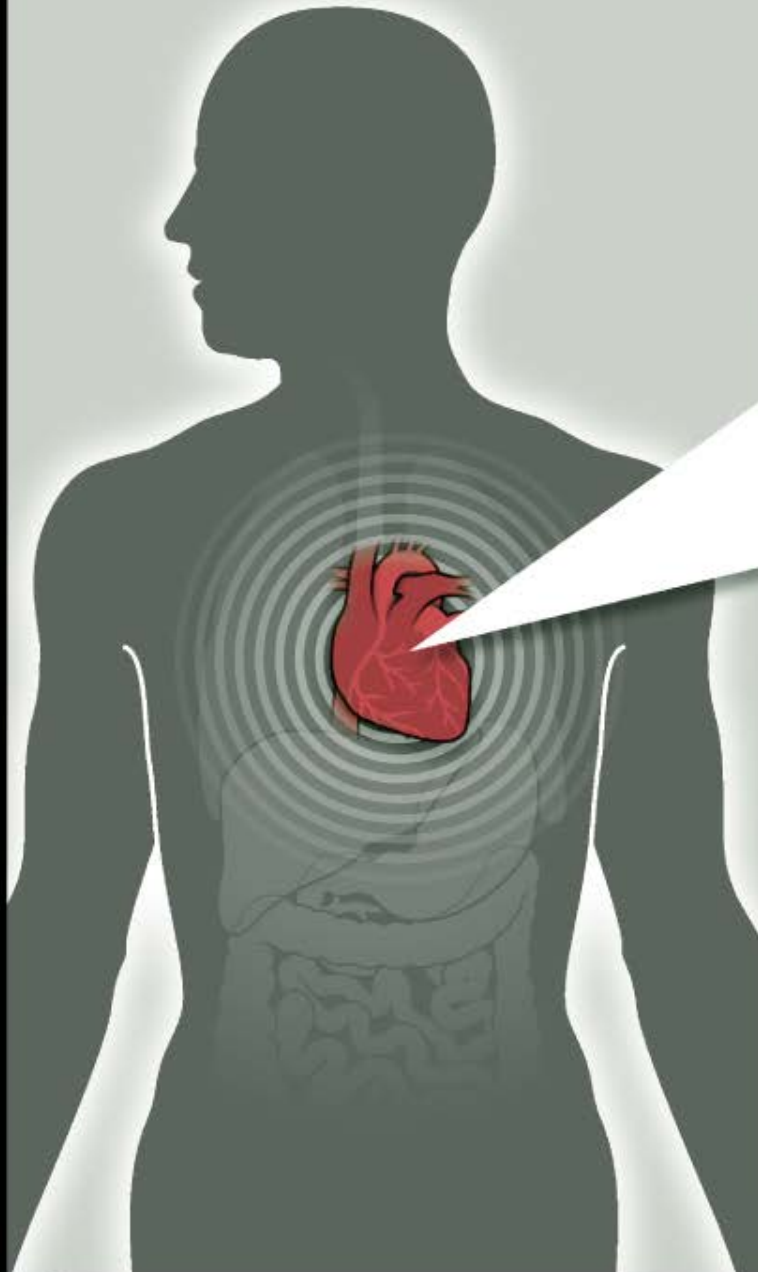
Trigger is activated and sends signal to heart to beat faster.

Trigger
Norepinephrine

Beta₁
Receptor



Beta₁ Adrenergic Receptors in the Heart

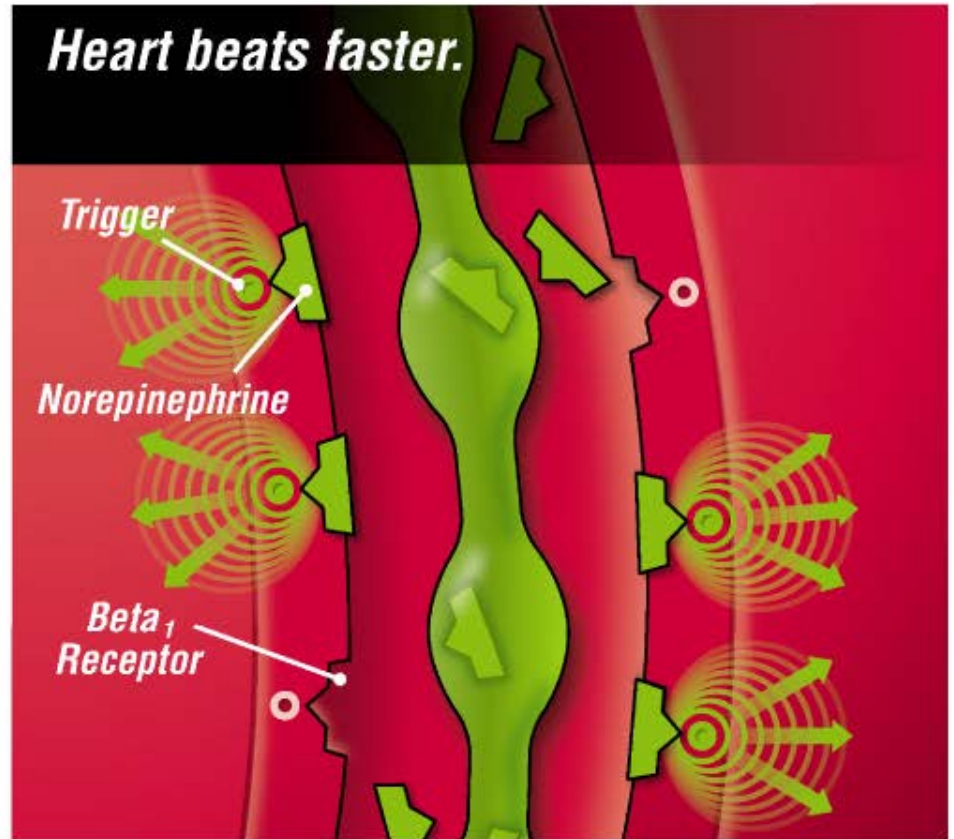


Heart beats faster.

Trigger

Norepinephrine

*Beta₁
Receptor*

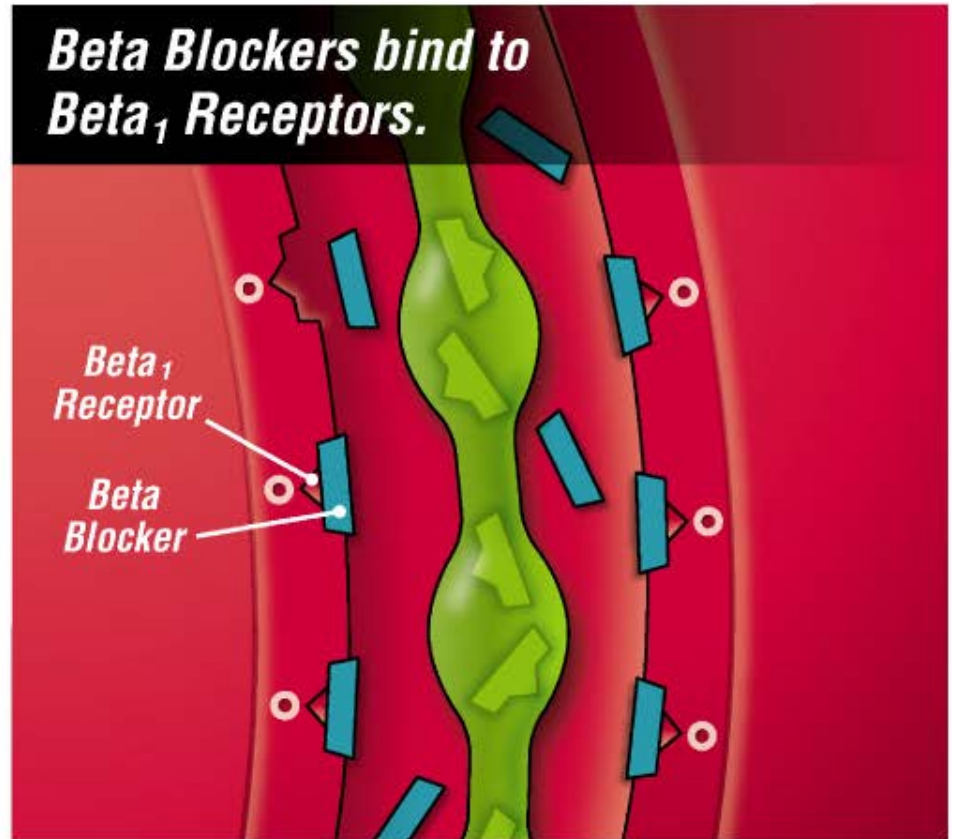
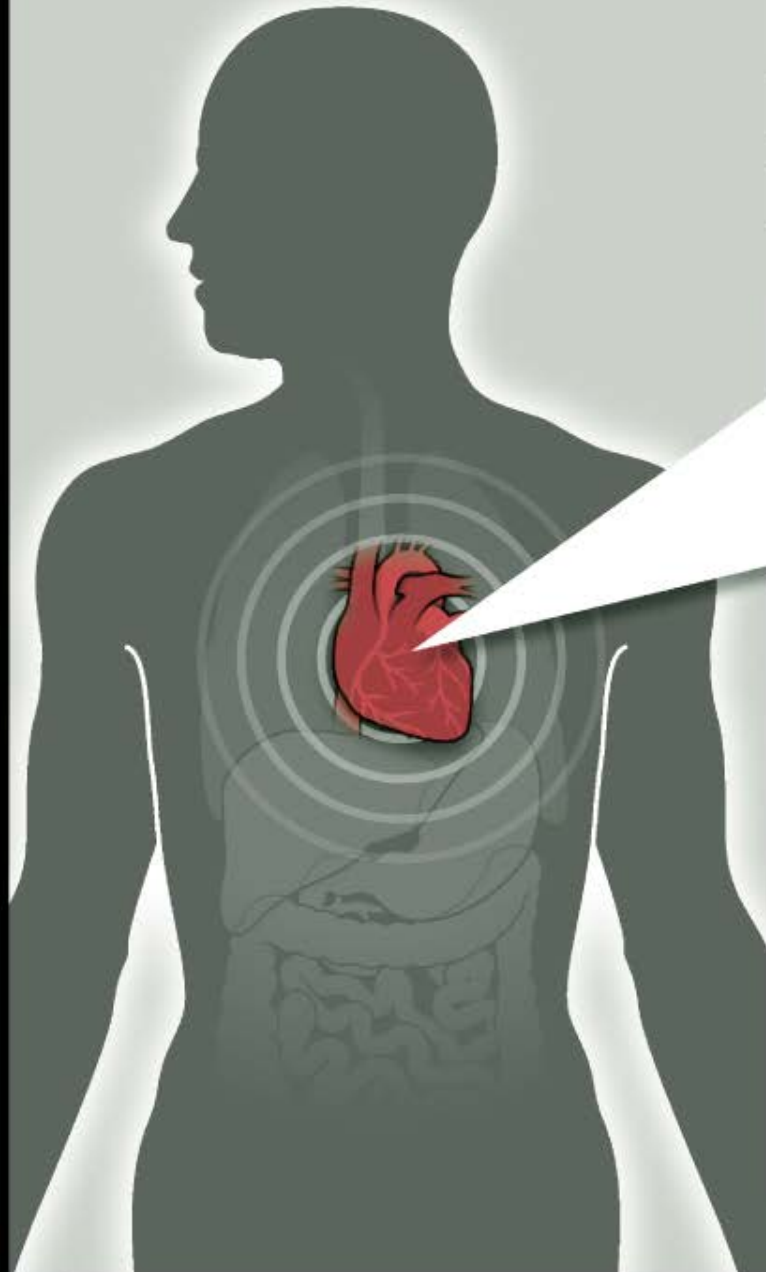


Beta Blockers Prevent Norepinephrine from Binding to Beta₁ Receptors

Beta Blockers bind to Beta₁ Receptors.

Beta₁ Receptor

Beta Blocker



Beta Blockers Prevent Norepinephrine from Binding to Beta₁ Receptors

Norepinephrine cannot bind to the Beta₁ Receptor.

Beta₁ Receptor

Beta Blocker

Norepinephrine

Beta Blockers Prevent Norepinephrine from Binding to Beta₁ Receptors

***NO SIGNAL* is sent to heart.
*Increase in heart rate is limited.***

*Beta₁
Receptor*

*Beta
Blocker*

Norepinephrine

A Medicine Is About More Than an Active Ingredient



It ***DELIVERS*** the Active Ingredient

- Safely
- Effectively
- Over the Desired Time Course

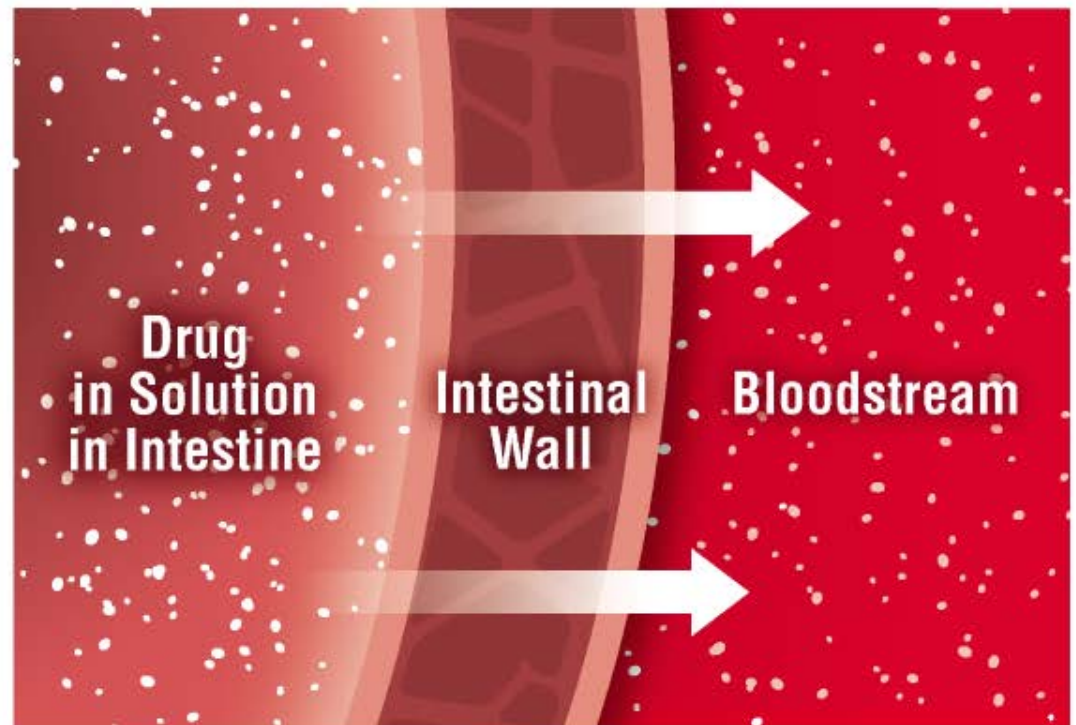
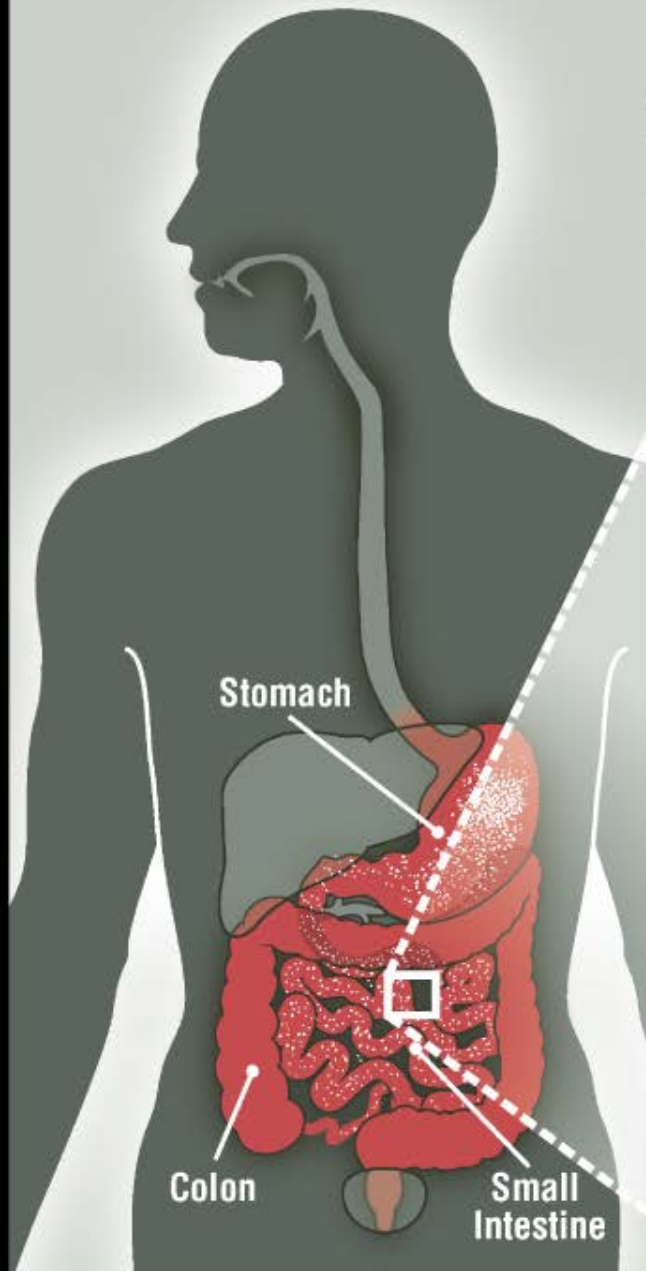
A Medicine Is About More Than an Active Ingredient



It Also Contains ***INACTIVE INGREDIENTS*** (Excipients)

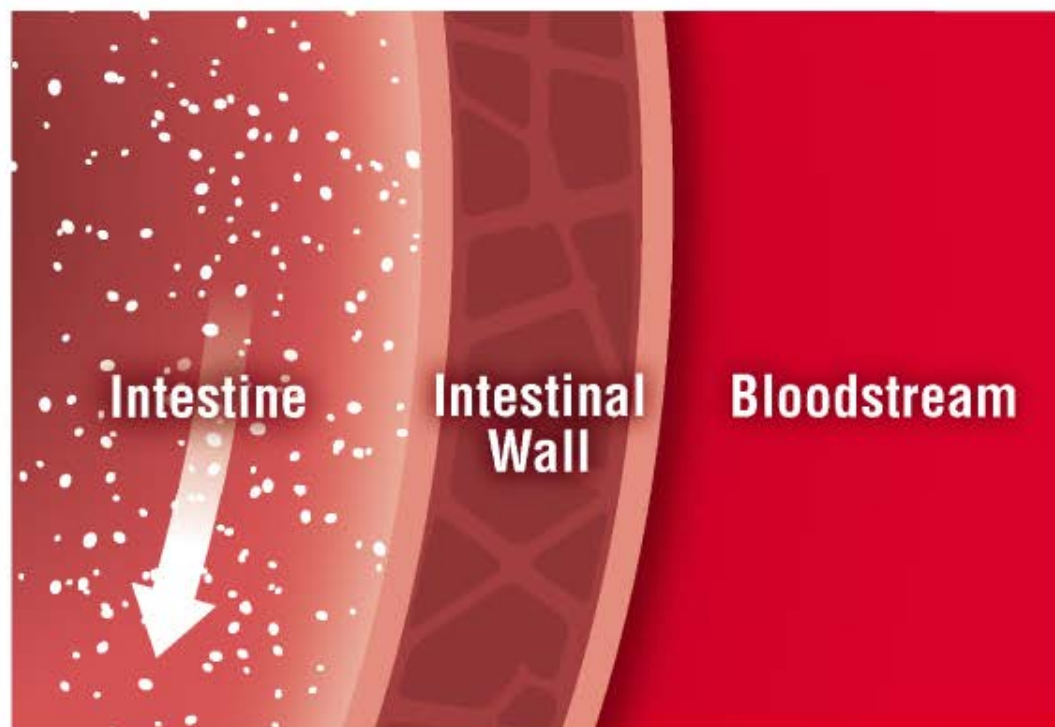
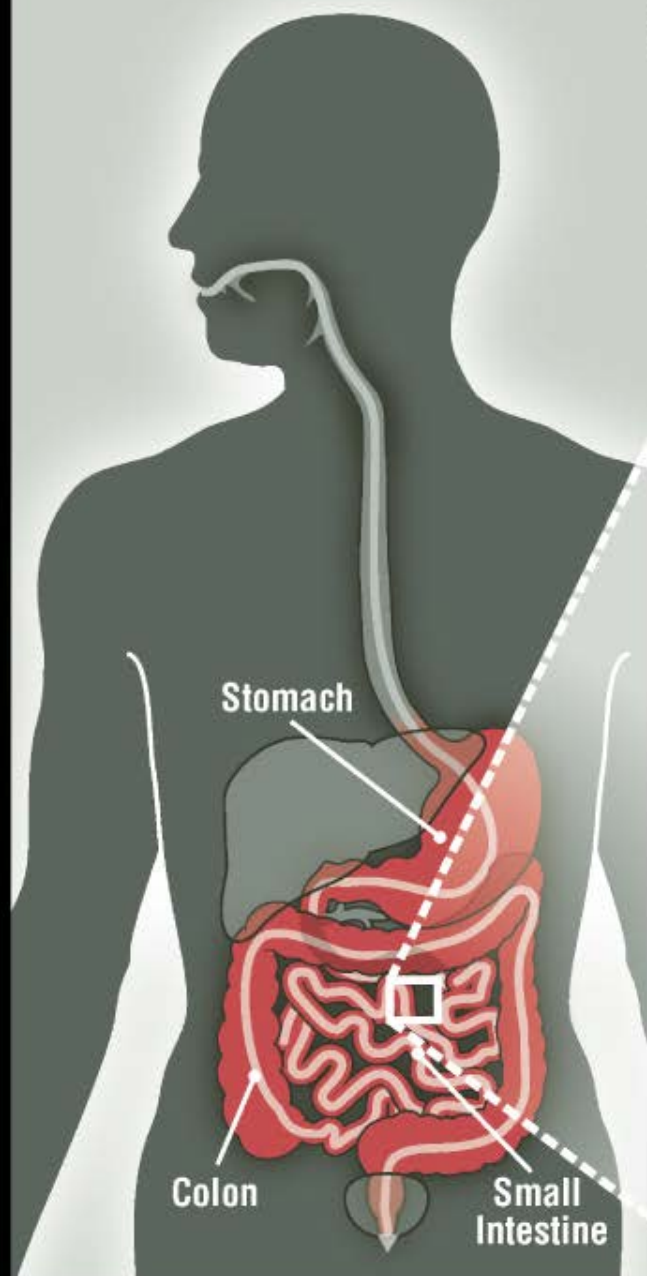
In Order for a Drug that Is Given Orally to Work the Active Must:

- 1. Dissolve in the GI tract***
- 2. Absorb into the bloodstream***



Solubility Is Important Because

- *If **NOT SOLUBLE**,
drug will **NOT BE ABSORBED***

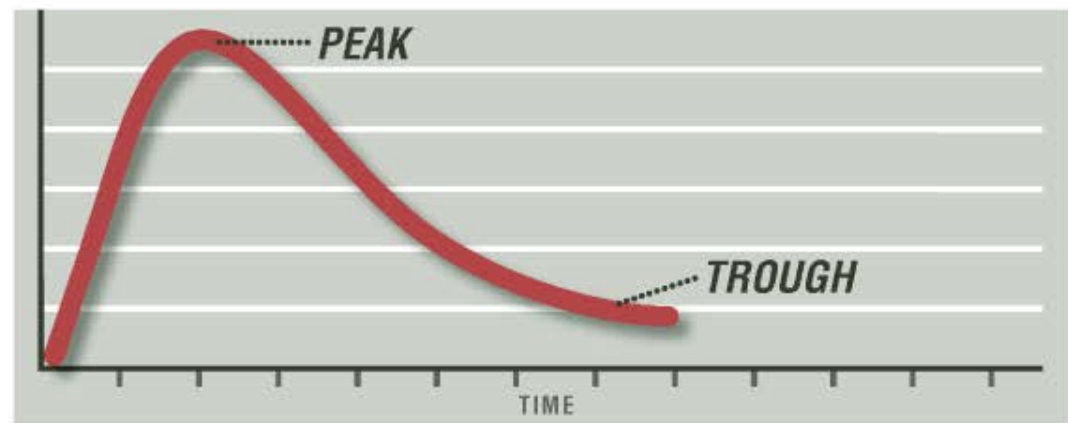


Immediate (Conventional) Release Dosage Form

IMMEDIATE RELEASE



PLASMA CONCENTRATION



Stomach

Colon

Small Intestine

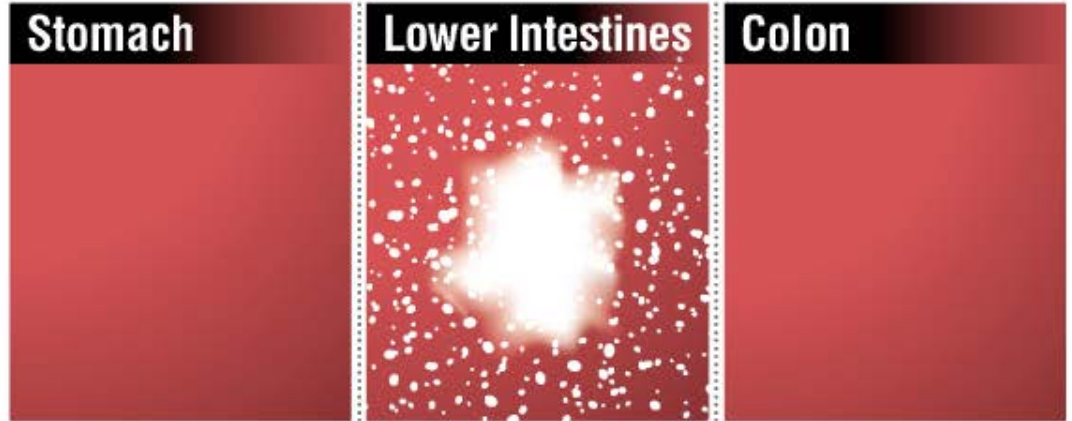
Delayed Release Dosage Form

DELAYED RELEASE

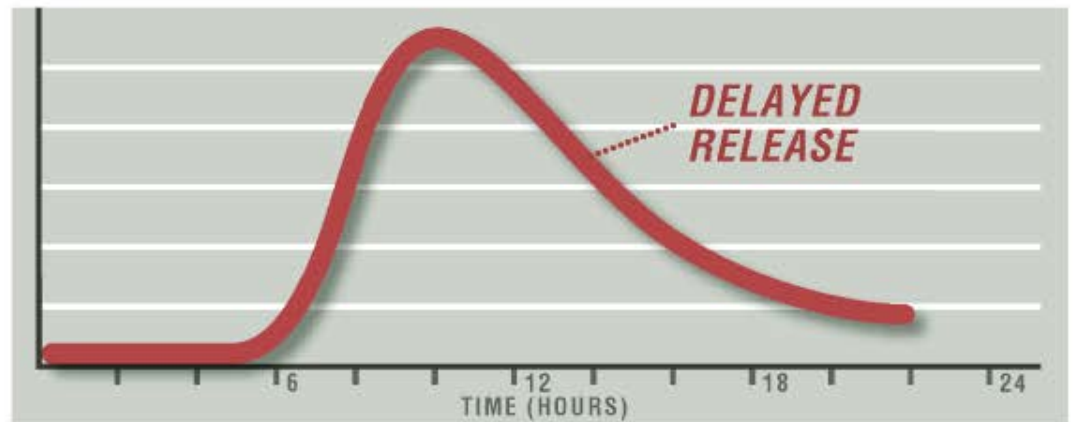
Stomach

Lower Intestines

Colon



PLASMA CONCENTRATION



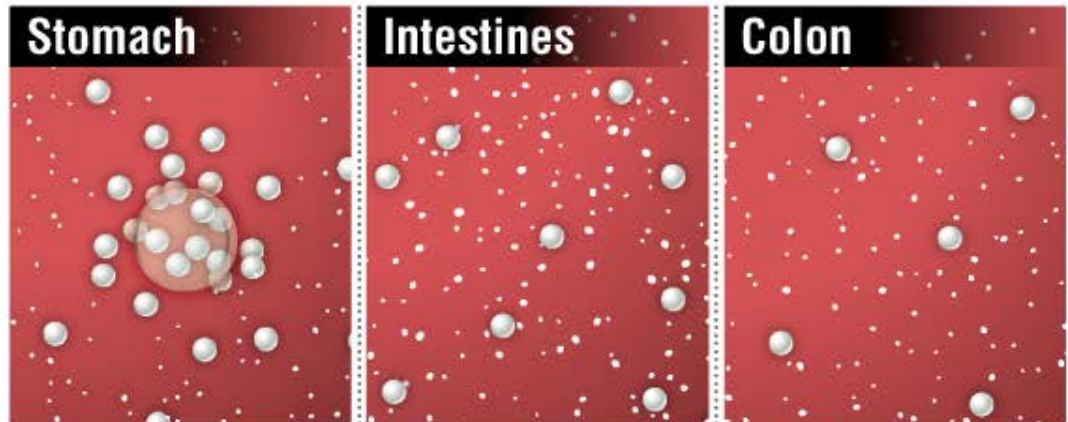
Stomach

Colon

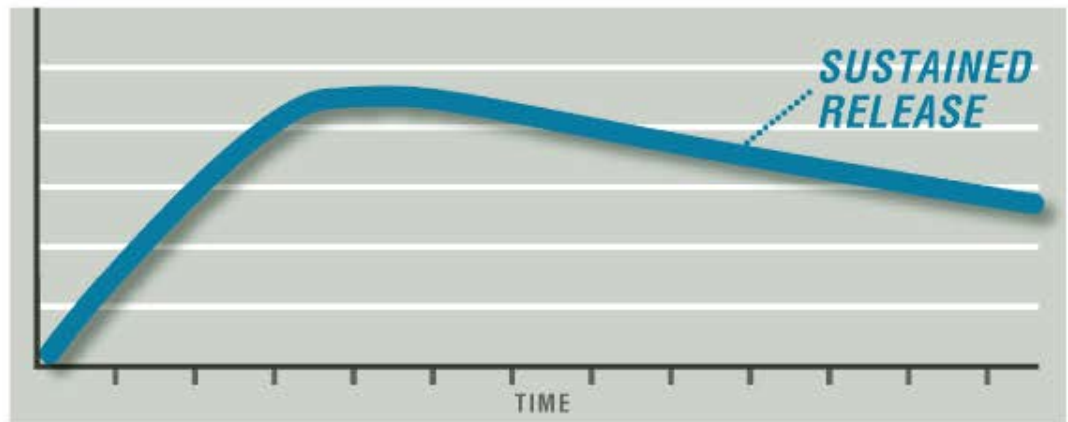
Small Intestine

Sustained Release Dosage Form

SUSTAINED RELEASE



PLASMA CONCENTRATION



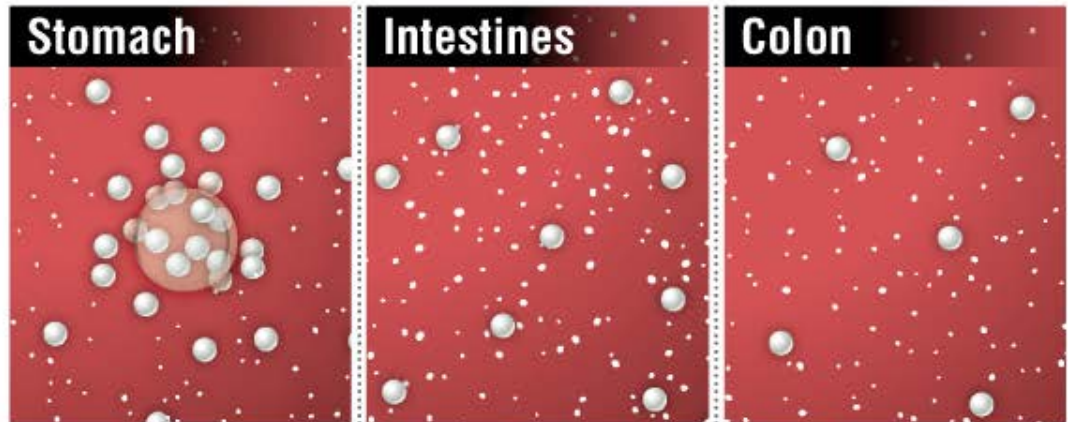
Stomach

Colon

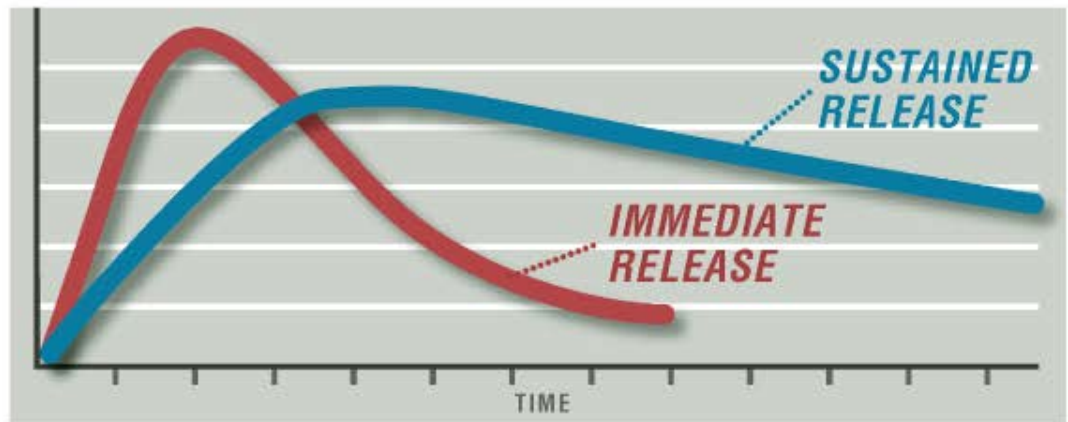
Small Intestine

Sustained Release Dosage Form

SUSTAINED RELEASE



PLASMA CONCENTRATION

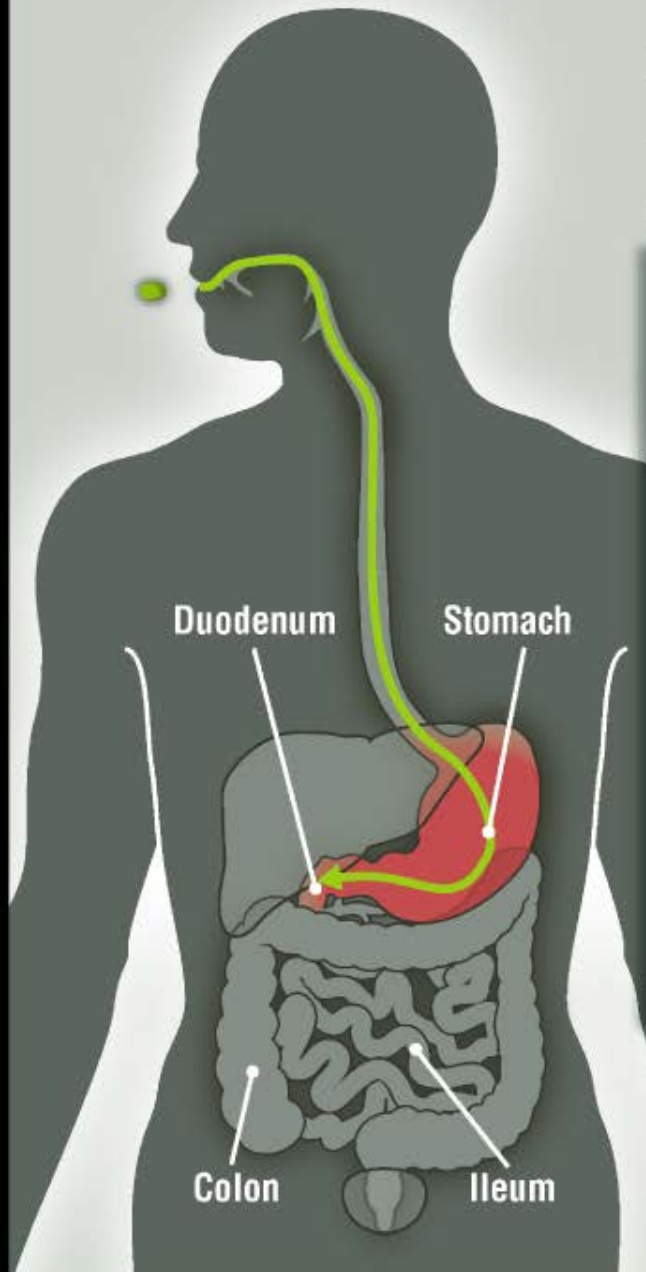


Stomach

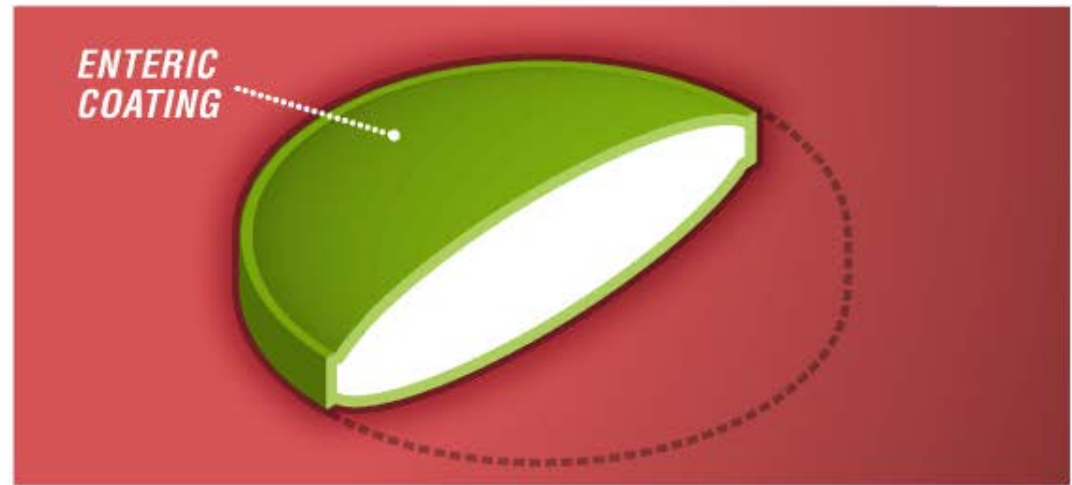
Colon

Small Intestine

Delayed (Enteric) Release Dosage Form



*Enteric coating does not dissolve in the **acidic environment** of the stomach or duodenum*



Delayed (Enteric) Release Dosage Form

*Release is delayed until the coating is dissolved in the somewhat **basic environment** of the lower GI tract*

Duodenum Stomach

Colon Ileum

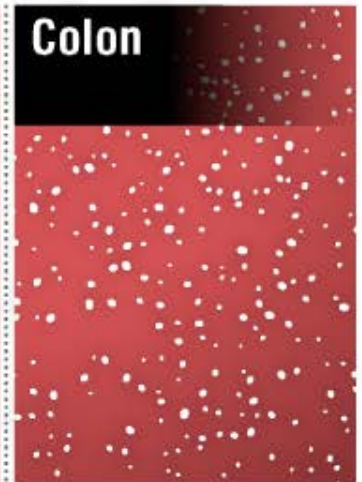
Stomach/
Duodenum



Ileum



Colon



Importance of pH Independence

pH DEPENDENT

Stomach

pH: 1.0 – 3.5



Duodenum

pH: 5.0 – 6.0



Ileum/Colon

pH: 7.0 – 8.0



pH INDEPENDENT

Stomach

pH: 1.0 – 3.5



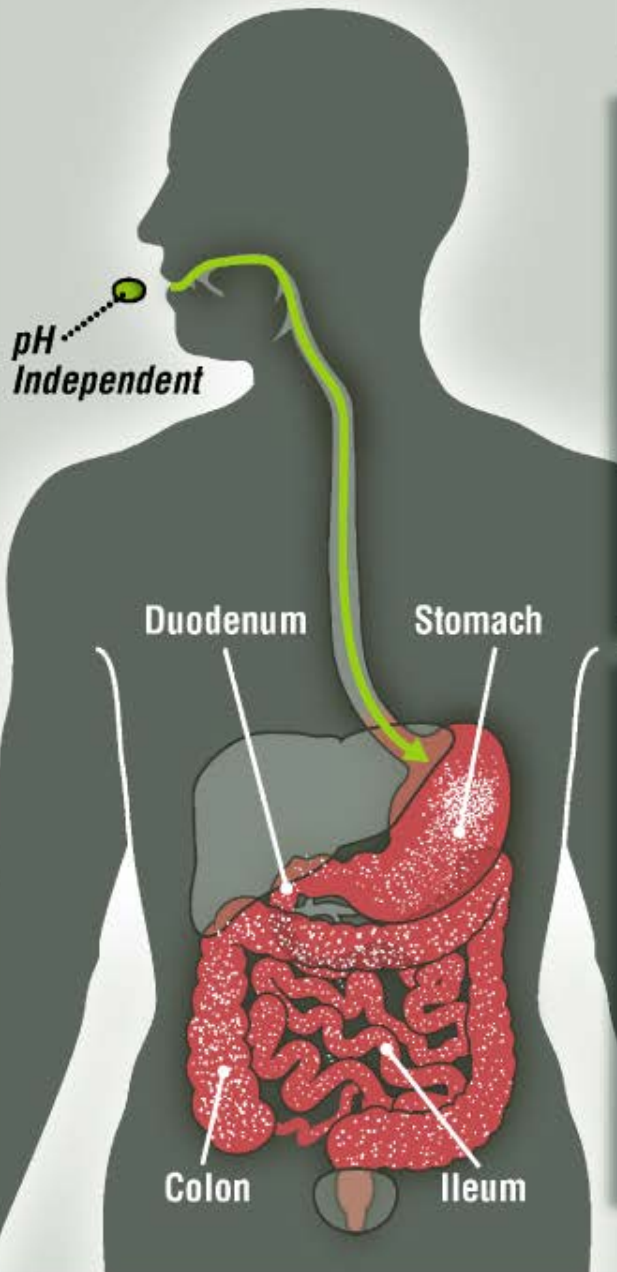
Duodenum

pH: 5.0 – 6.0



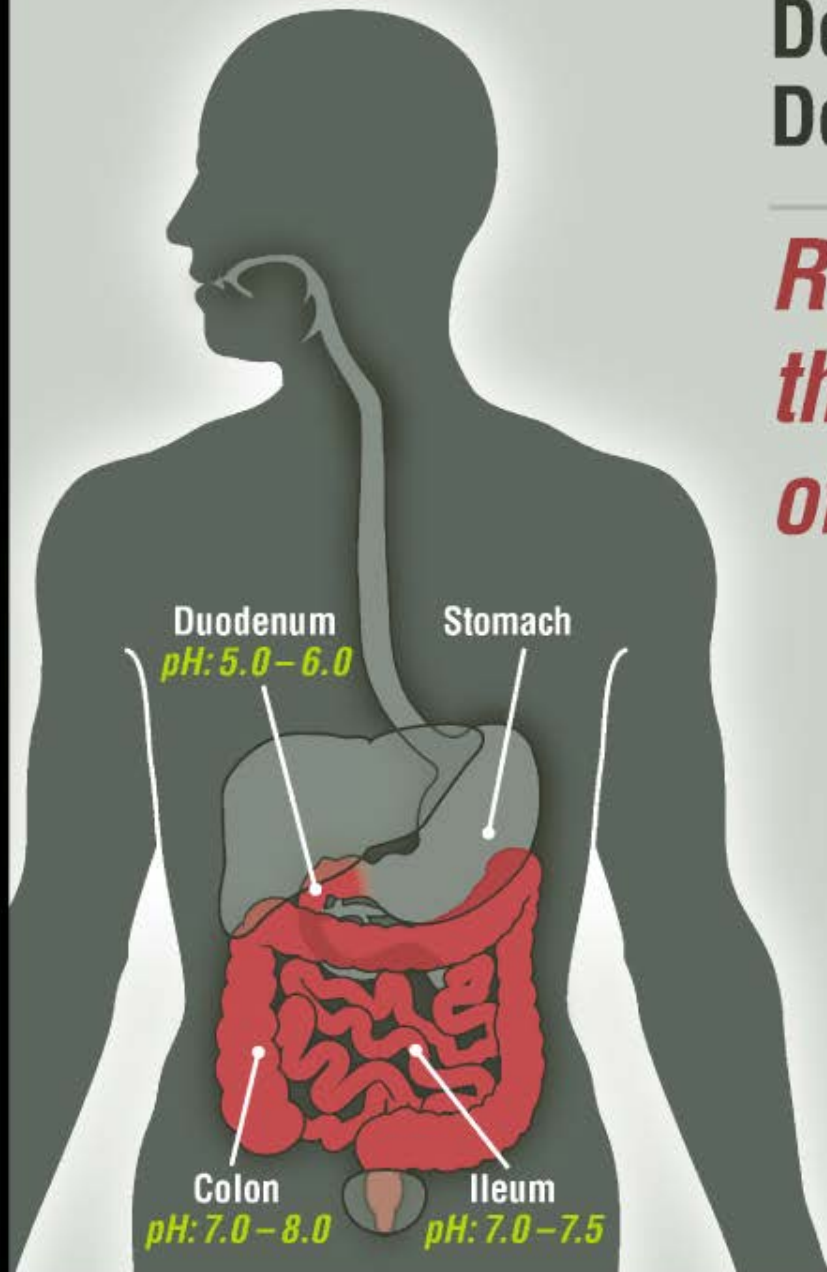
Ileum/Colon

pH: 7.0 – 8.0

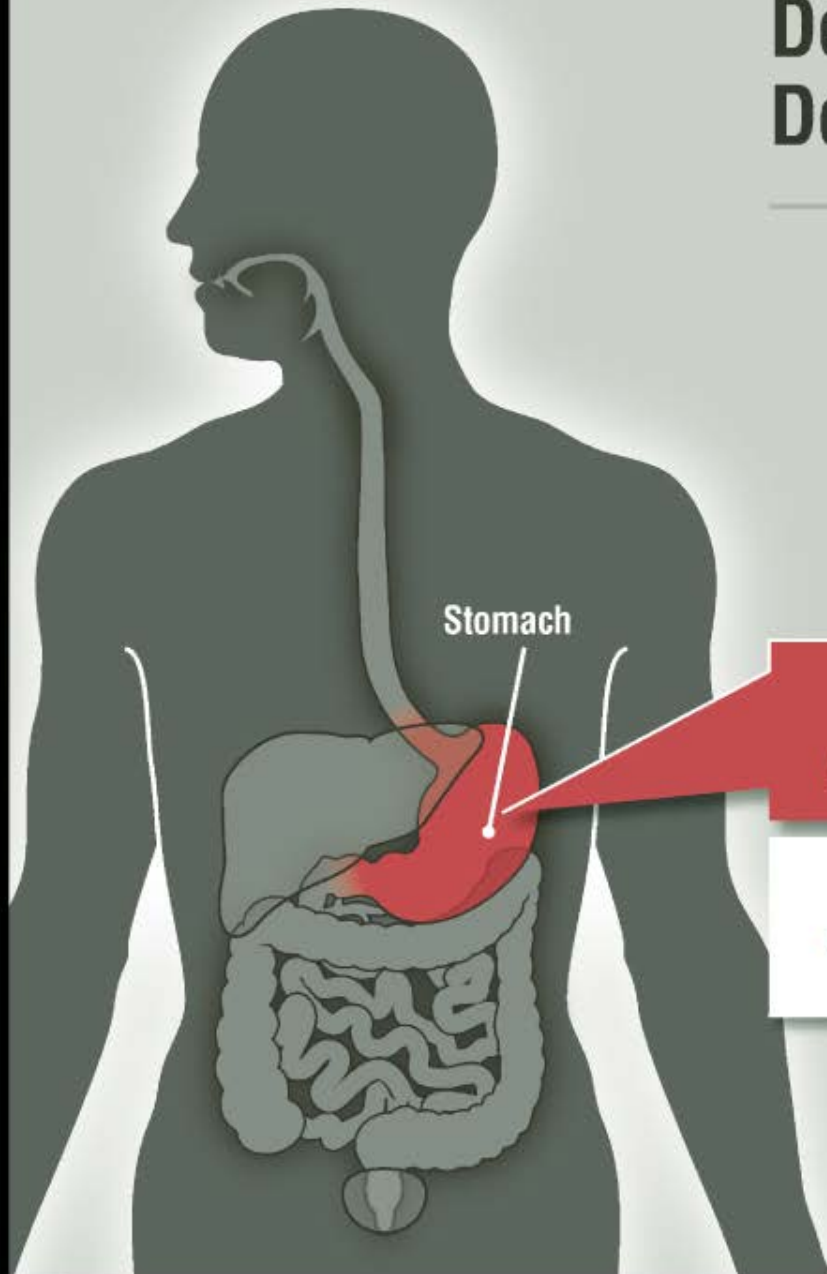


Delayed (Enteric) Release Dosage Form

Release is dependent on the acidity conditions (pH) of the GI tract.



Delayed (Enteric) Release Dosage Form

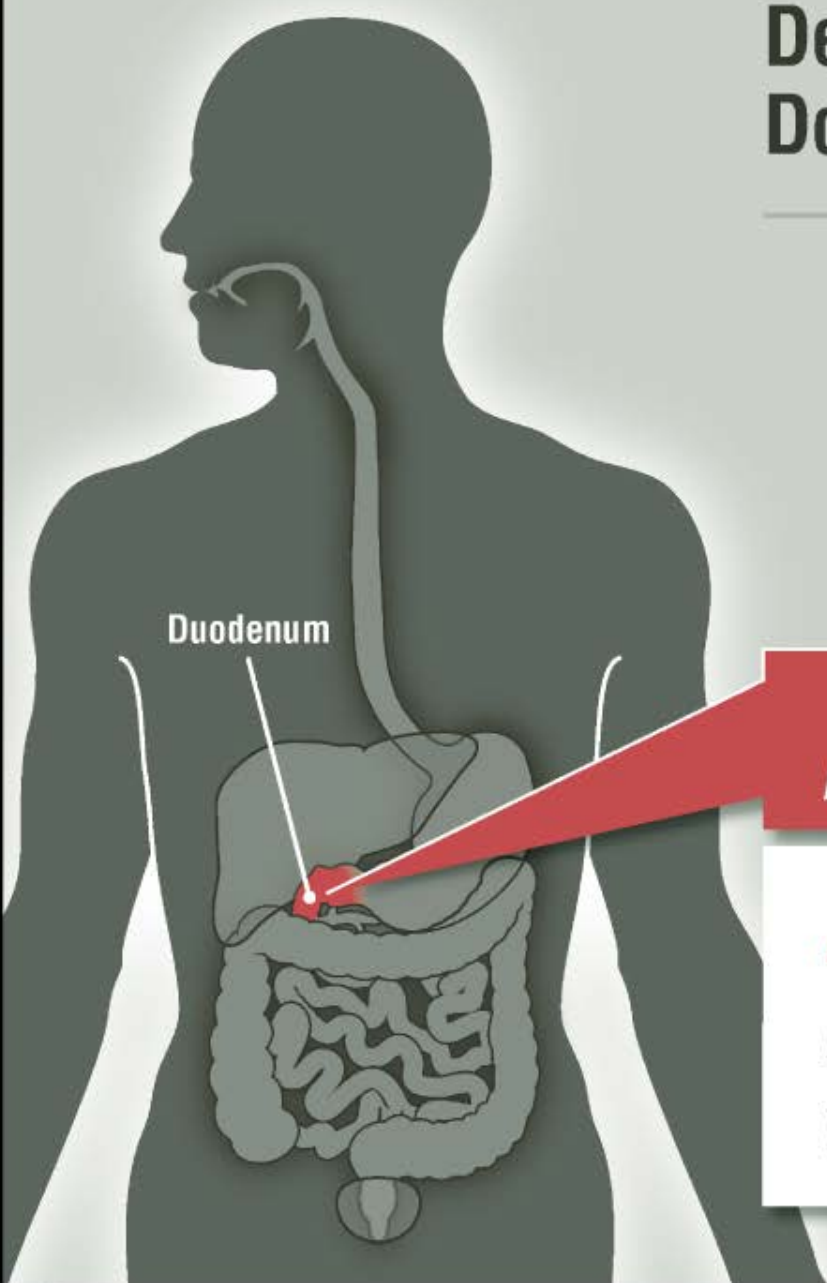


Stomach

$pH = 1.0 - 3.5$

Stomach is highly acidic.

Delayed (Enteric) Release Dosage Form

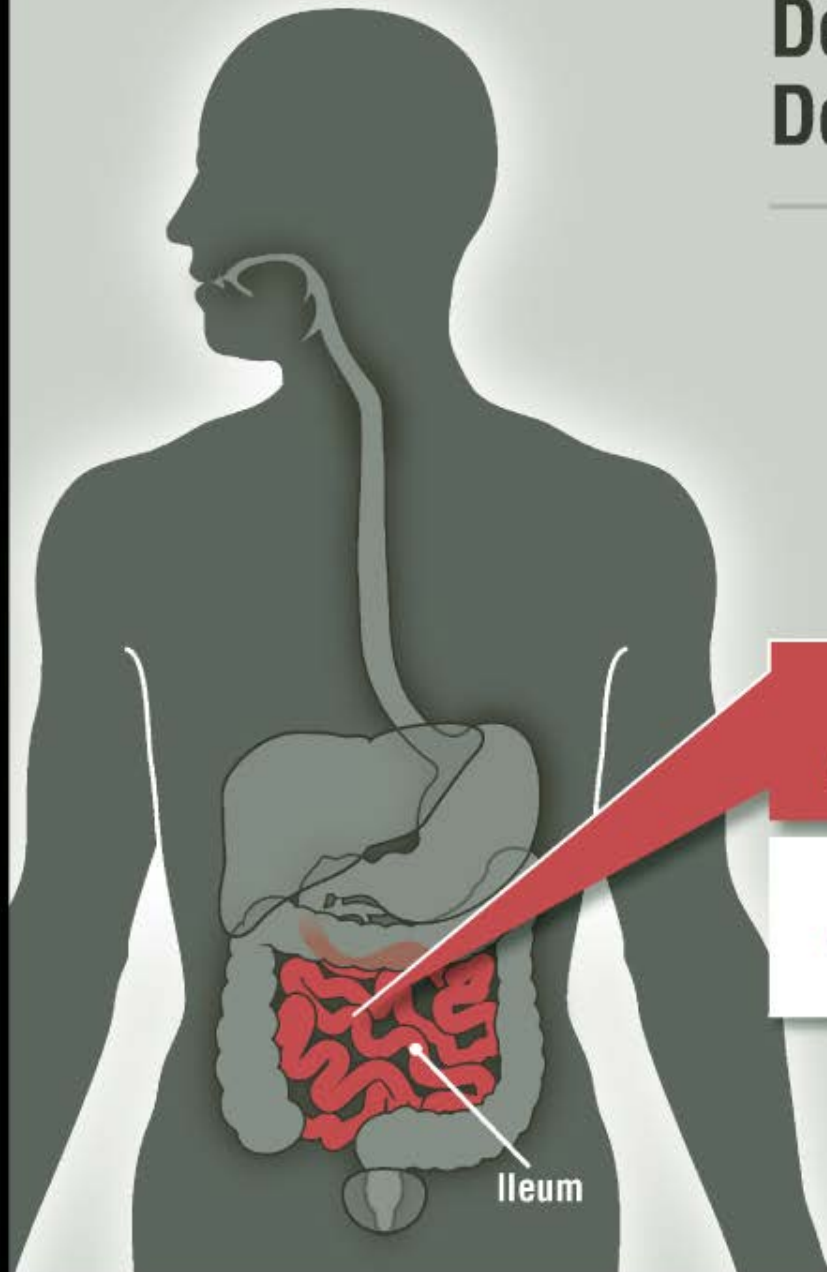


Duodenum

pH = 5.0 – 6.0

Duodenum (upper small intestine) is less acidic than the stomach.

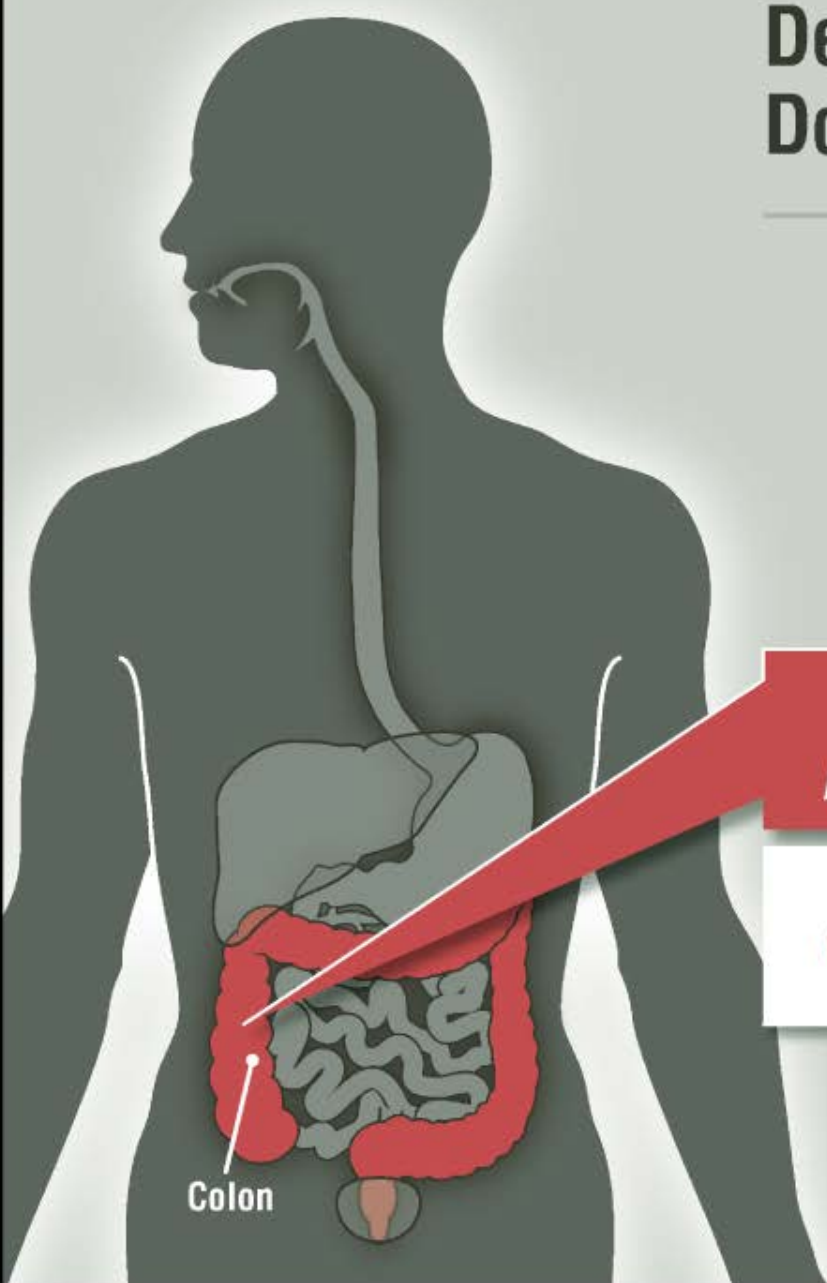
Delayed (Enteric) Release Dosage Form



pH = 7.0 – 7.5

Ileum is somewhat basic.

Delayed (Enteric) Release Dosage Form

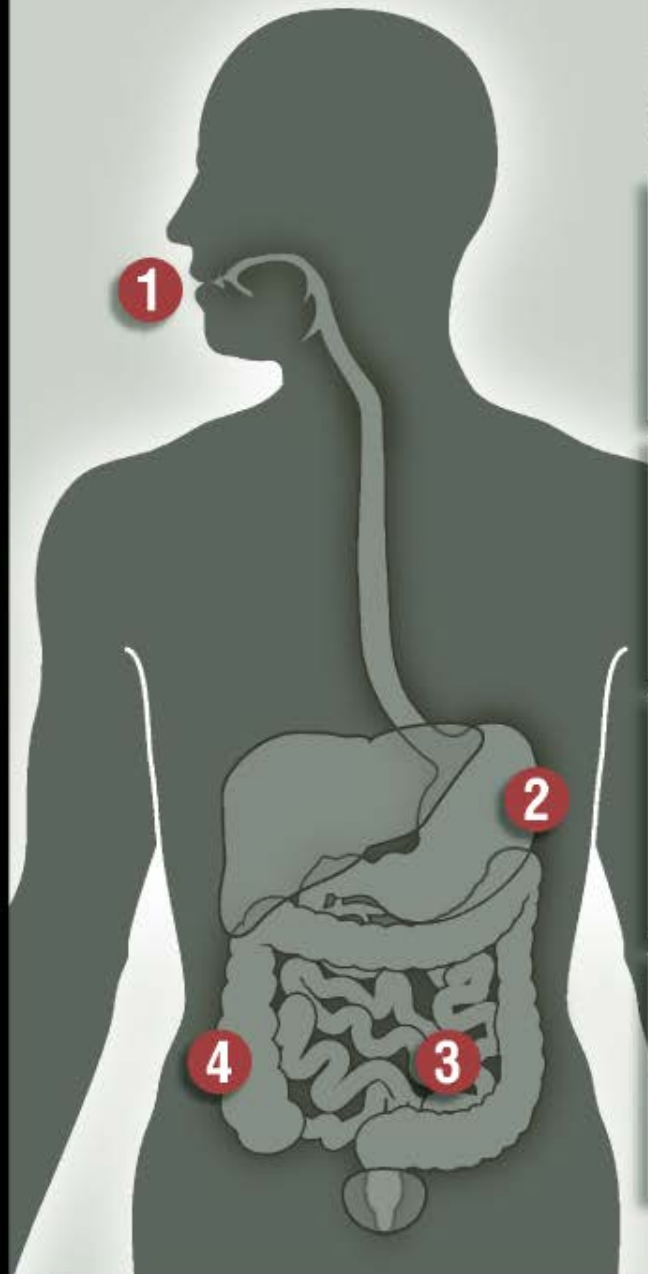


Colon

pH = 7.0 – 8.0

Colon is somewhat basic.

Examples of Sustained Release Systems



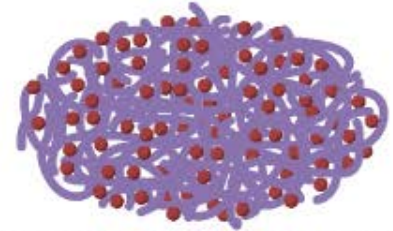
Insoluble Matrix

Eroding Matrix

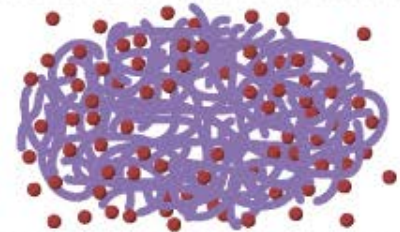
Film Coating

Osmotic System

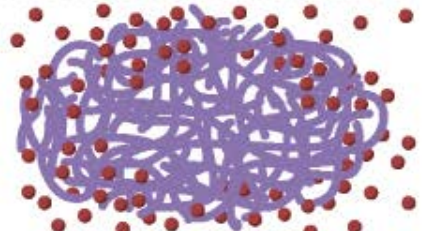
1
In the MOUTH



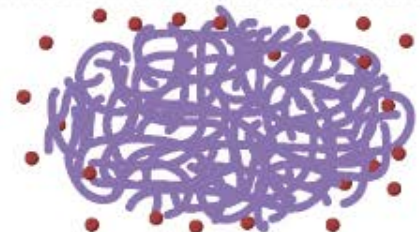
2
In the STOMACH



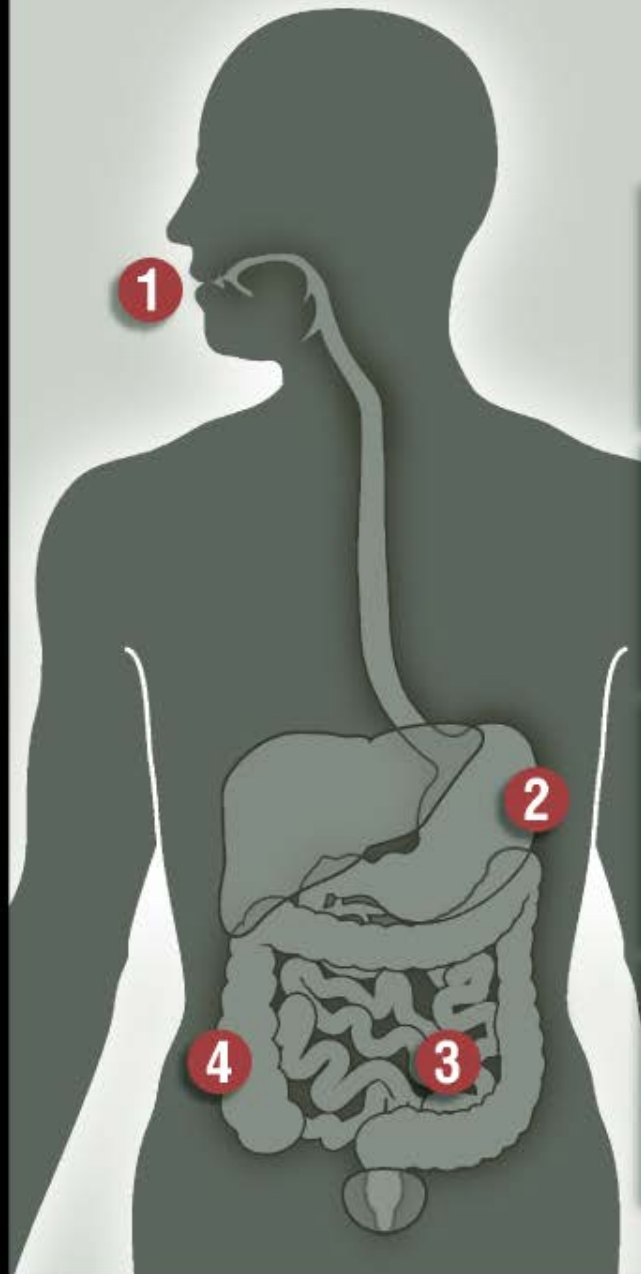
3
In the ILEUM



4
In the COLON



Examples of Sustained Release Systems



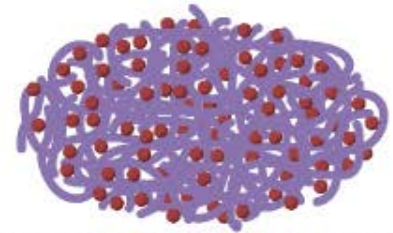
Insoluble Matrix

Eroding Matrix

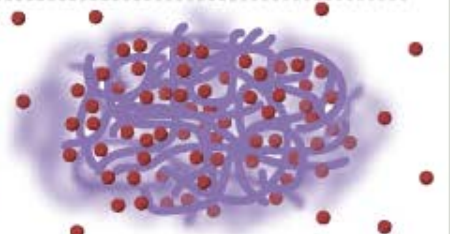
Film Coating

Osmotic System

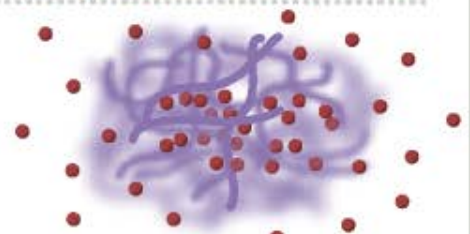
1
In the MOUTH



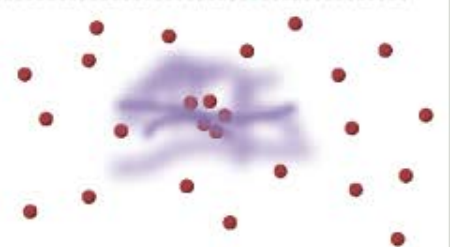
2
In the STOMACH



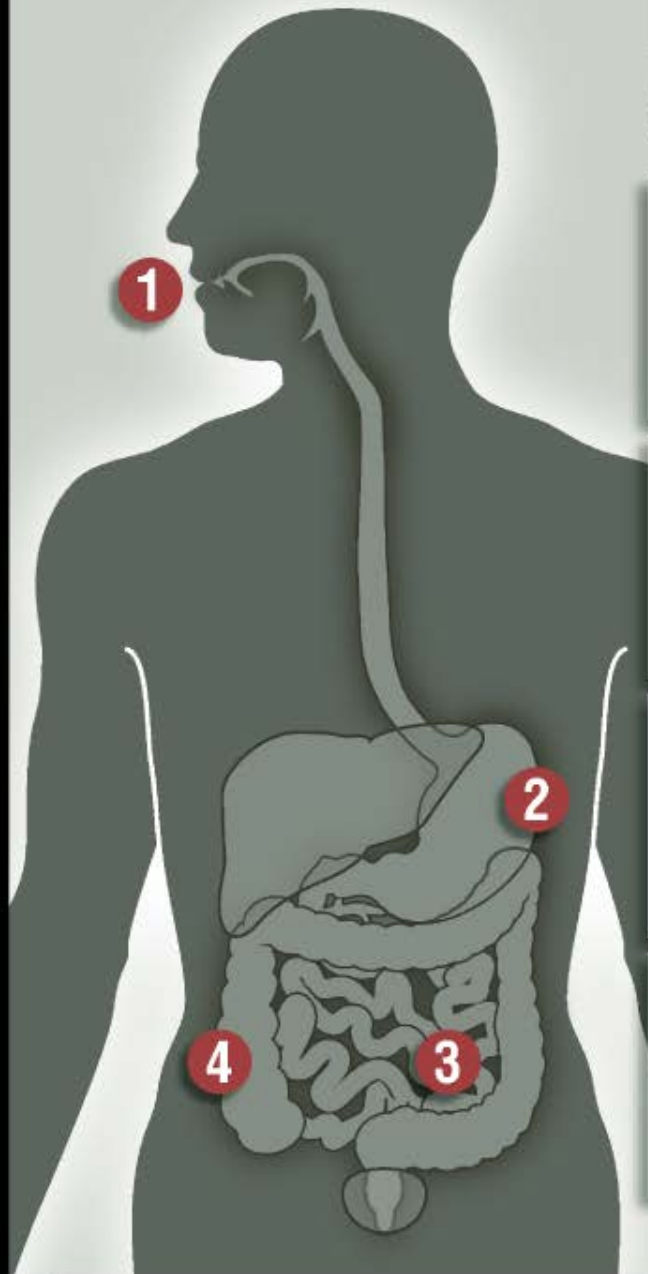
3
In the ILEUM



4
In the COLON



Examples of Sustained Release Systems



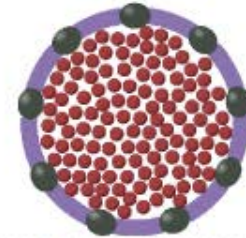
Insoluble Matrix

Eroding Matrix

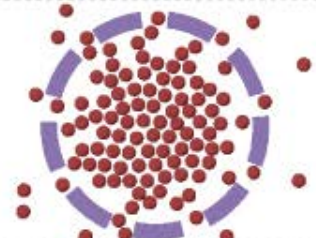
Film Coating

Osmotic System

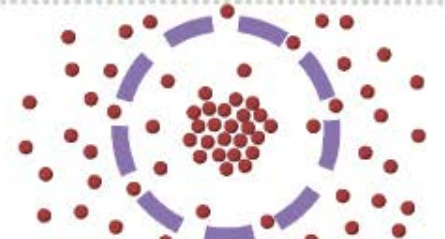
1
In the MOUTH



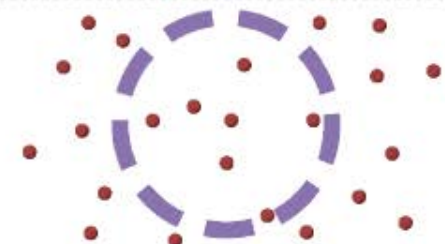
2
In the STOMACH



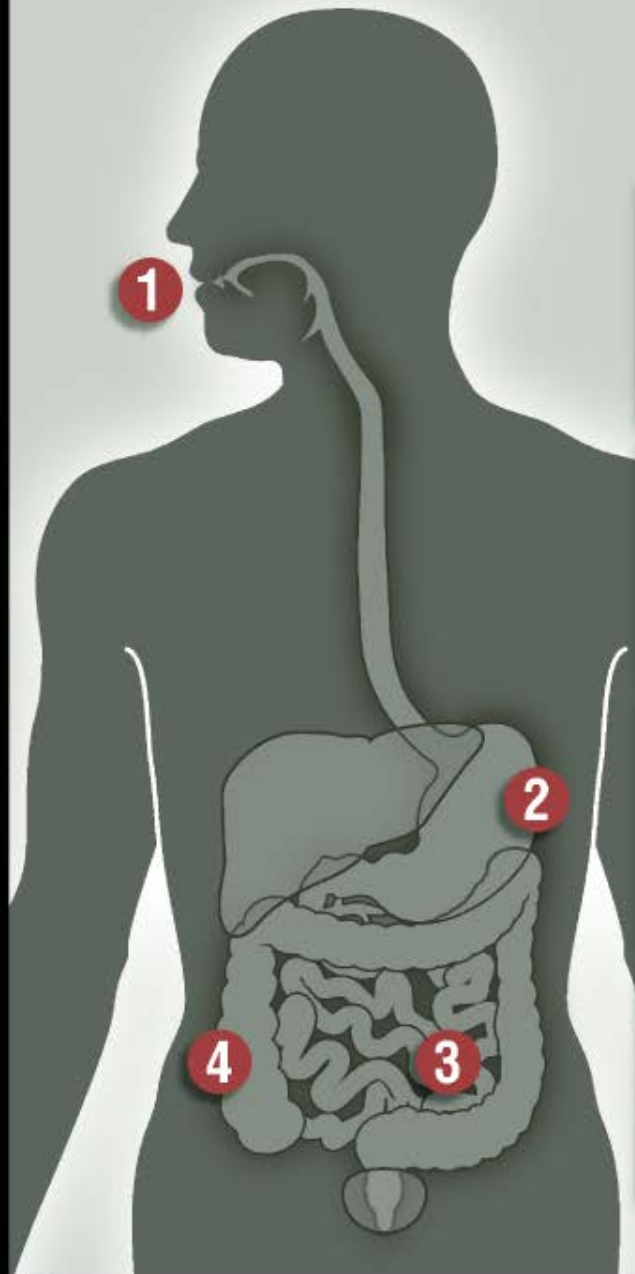
3
In the ILEUM



4
In the COLON



Examples of Sustained Release Systems



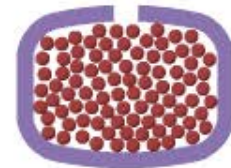
Insoluble Matrix

Eroding Matrix

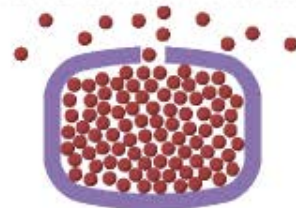
Film Coating

Osmotic System

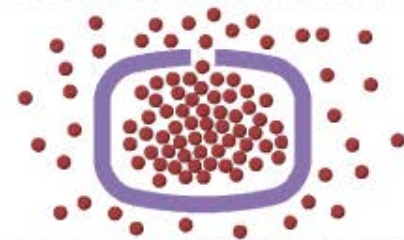
1
In the MOUTH



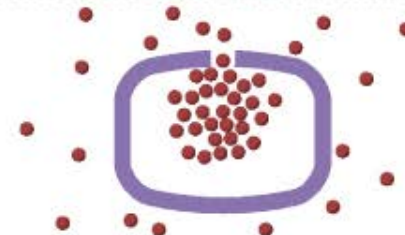
2
In the STOMACH



3
In the ILEUM



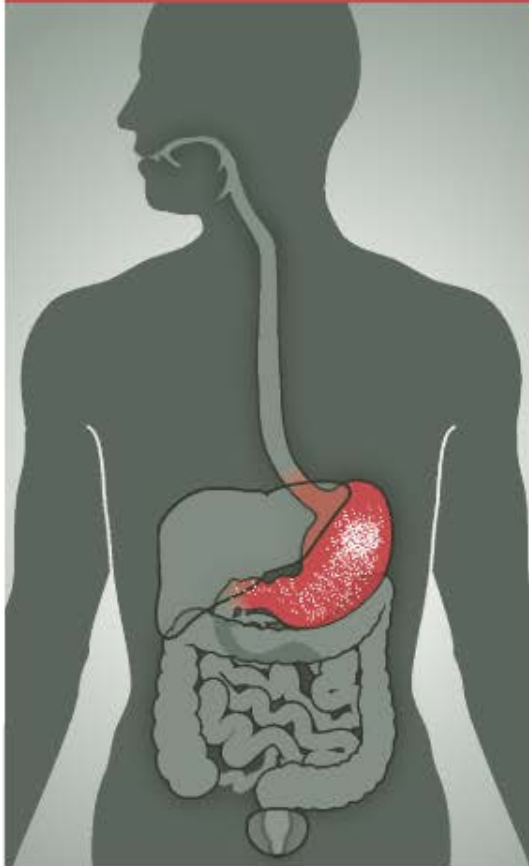
4
In the COLON



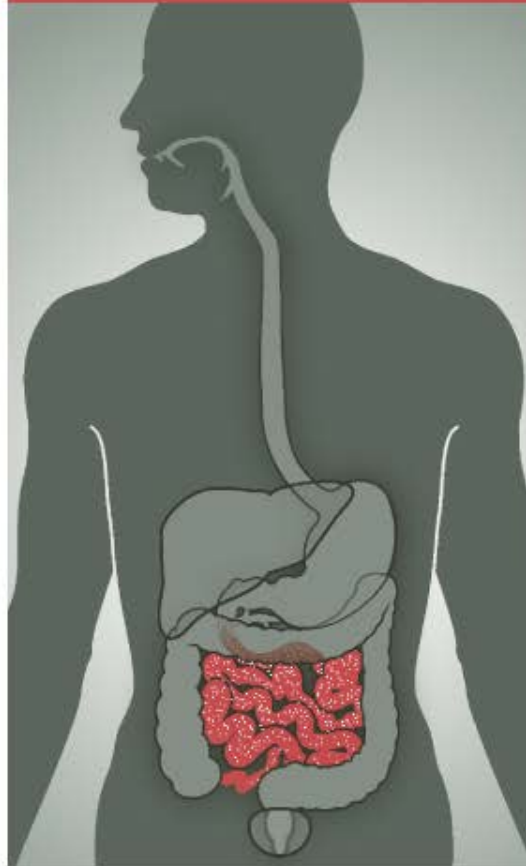
GI Transit Time

GENERALLY TAKES 24 HOURS

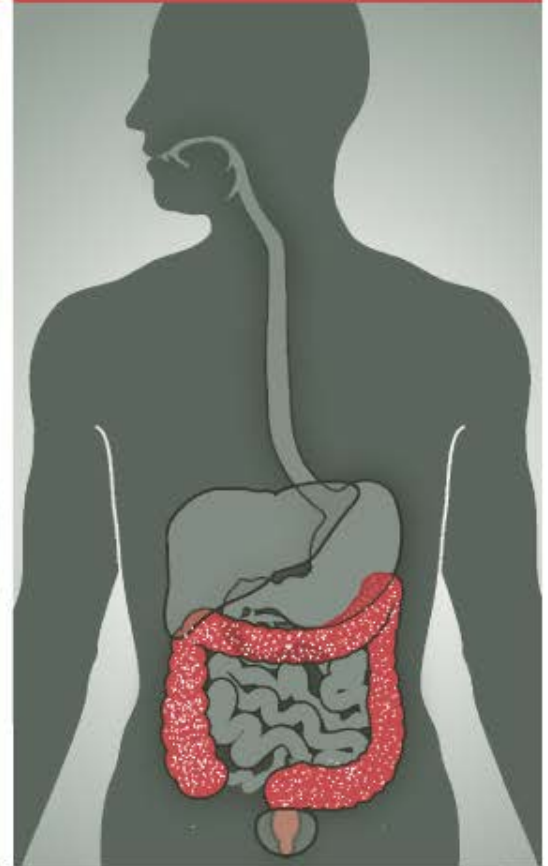
Leaves **STOMACH** within
1 – 6 HOURS



Resides in **SMALL INTESTINE**
3 – 5 HOURS

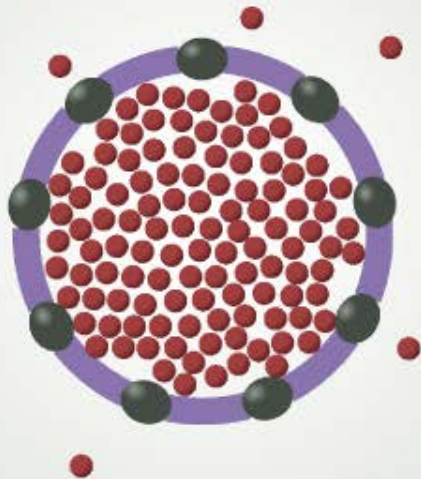


Arrives in **COLON** After
5 – 7 HOURS

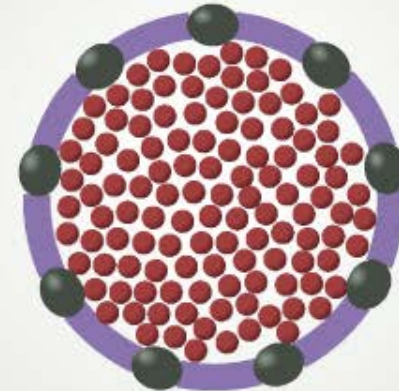


Salt Solubility Affects the Rate of Release

HIGH Solubility



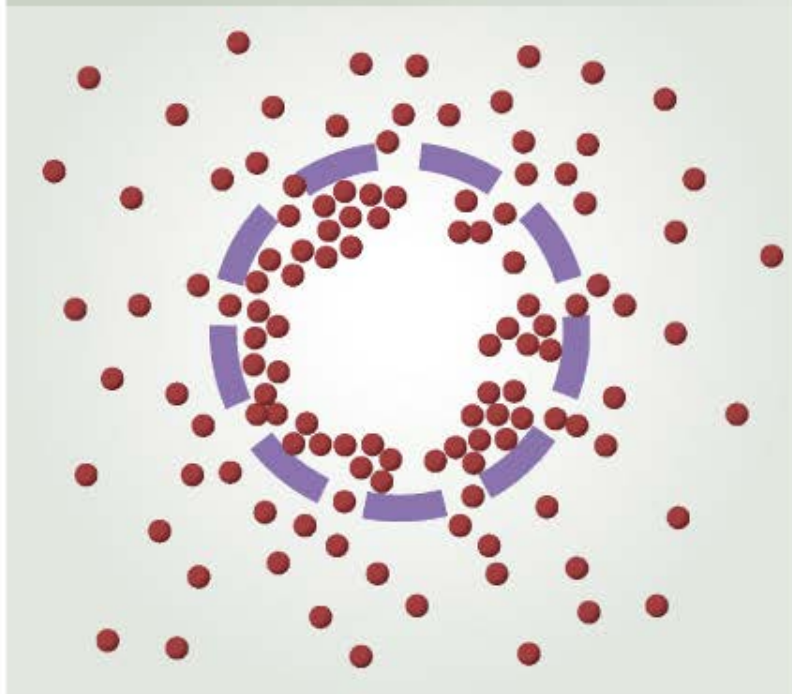
LOW Solubility



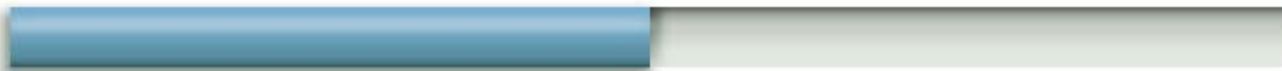
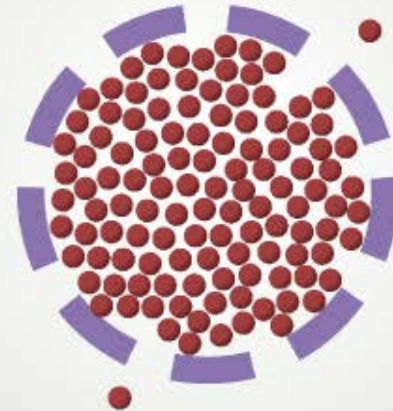
E L A P S E D T I M E

Salt Solubility Affects the Rate of Release

HIGH Solubility

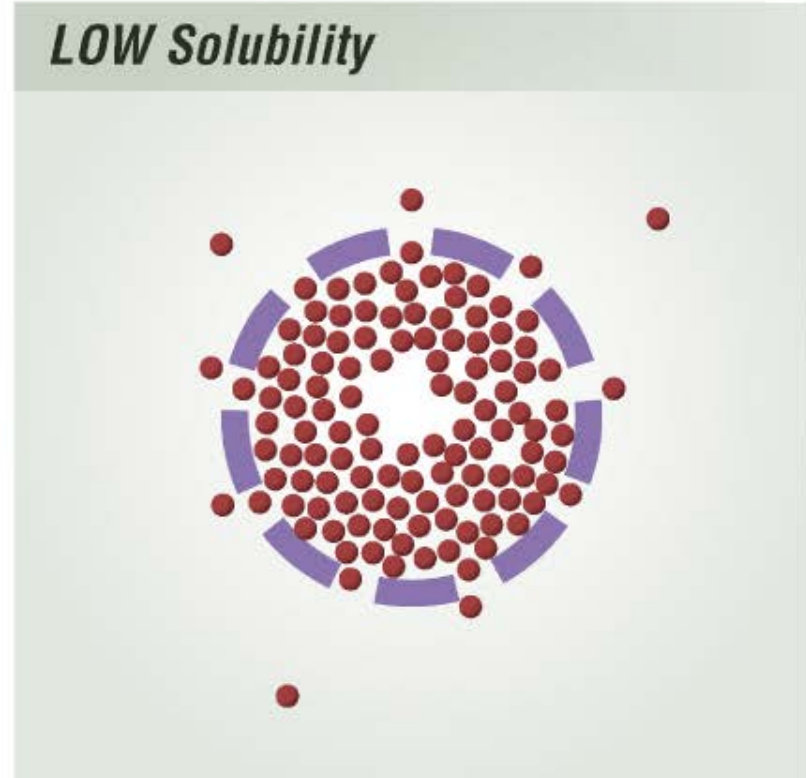
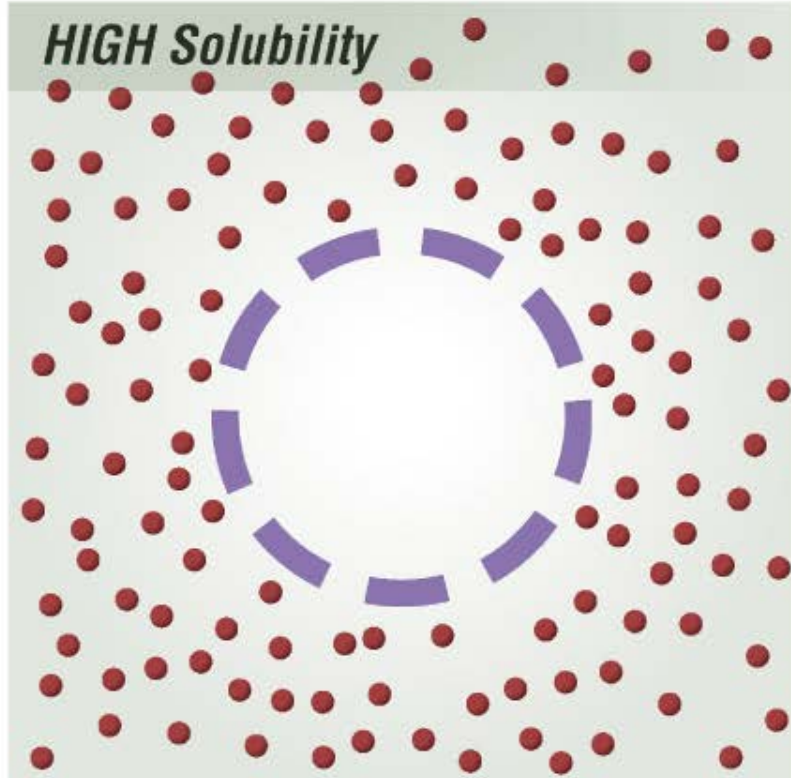


LOW Solubility



E L A P S E D T I M E

Salt Solubility Affects the Rate of Release



E L A P S E D T I M E

Salt Solubility Affects the Rate of Release

HIGH Solubility

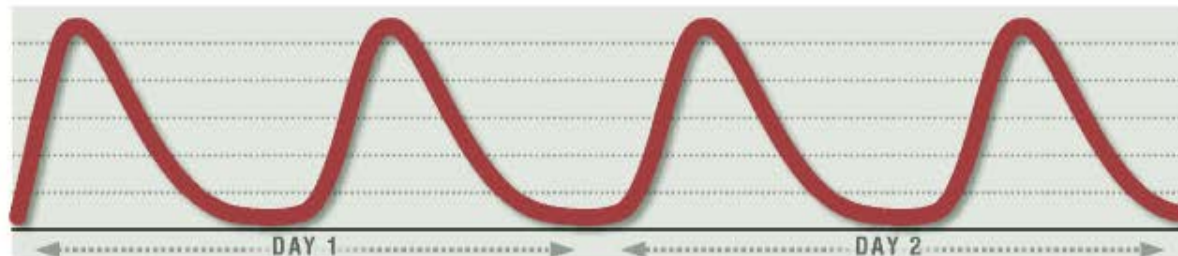


LOW Solubility

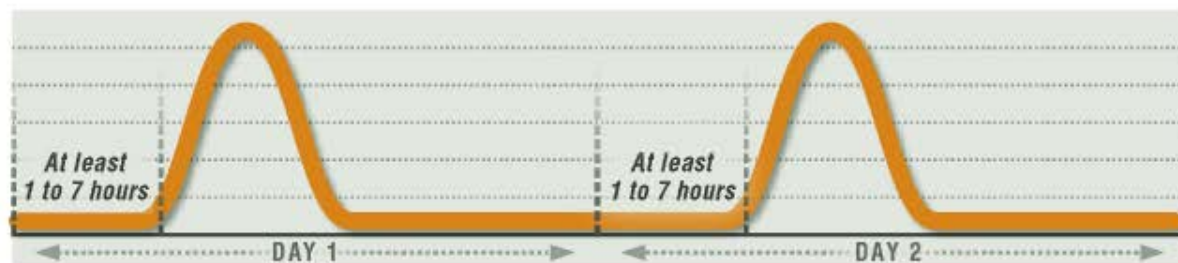


Multiple Dosing

**IMMEDIATE
RELEASE:**
*Twice Daily
Dosing*



**DELAYED
RELEASE:**
*Once Daily
Dosing*



**SUSTAINED
RELEASE:**
*Once Daily
Dosing*

