

2 GOOD™

AMOXICILLIN MODIFIED RELEASE TABLETS WITH TWICE DAILY DOSAGE LEADING TO GREATER PATIENT COMPLIANCE

1. Introduction

Amoxicillin is a semi-synthetic antibiotic, an analog of ampicillin, with a broad spectrum of bacterial activity against many gram-positive and gram-negative microorganisms. **2 Good™** is a sustained release formulation of Amoxicillin that has been designed to provide therapeutically effective levels of the drug over extended periods without comprising on the bioavailability of the drug under fed or fasted conditions.

2. Medical Need

As opposed to the thrice daily dosing of conventional Amoxicillin formulations, **2 Good™** offers the convenience of twice a day dosing. This improves patient compliance, as there is no inconvenient mid-day dosing

3. Drug delivery system

The formulation is a rapidly disintegrating, muco-adhesive sustained release formulation that has been designed to localize the drug in the upper part of gastrointestinal tract, from where the absorption of Amoxicillin is highest.

The drug delivery system for this drug is based on the principles of muco-adhesion between gastric mucosa and drug containing polymer particles. The delivery system on reaching the stomach rapidly disintegrates into small particles. These particles have mucin-binding property and adhere to the mucosal surface. This rapid disintegration provide initial burst release and helps in achieving the MIC levels within 1-2 hours. Due to retention of drug in upper GIT, lesser unabsorbed drug reaches the colon and therefore

the incidence of diarrhea is likely to be significantly reduced. The formulation has been designed to achieve time above MIC (T/MIC) of at least 40%.

4. Clinical Experience

A pilot pharmacokinetic study was conducted in 6 healthy volunteers to determine the bioavailability of amoxicillin MR 750 mg BD (1500 mg/day) disintegrating type tablets. The design was multiple-dose, bioavailability (BA) study in healthy adult males under fed condition. Blood samples were taken at predetermined times (Pre-dose and at 1, 2, 4, 6, 8, 12, 13, 14, 16, 18, 20, and 24 h post first dose) and were analyzed for amoxicillin by a specific validated HPLC fluorescence method.

Results

The AUC₀₋₂₄ of the test formulation was 62.6 µg/ml.

Parameter (units)	1st Dose	2nd Dose	Average
C _{max} (µg/mL)	7.03 ± 3.05	4.43 ± 1.72	5.73 ± 2.72
T _{max} (hours)	2.67 ± 1.03	17.0 ± 2.45	--

Table 2: C_{max} (µg/mL) and Tmax (hours) of the test formulation

The T > MIC at various levels of plasma concentration are given in table 3:

	MIC					
	0.25 µg/ml	0.5 µg/ml	1 µg/ml	1.6 µg/ml	2 µg/ml	4 µg/ml
% T > MIC	99.48	92.71	83.33	66.67	58.33	15.83

Table 3: Percentage of time for which amoxicillin concentration is above reported MIC values

Conclusion

In the fed state BA study conducted for twice a day amoxicillin MR tablets 750 mg, it was observed that the time above an MIC of up to 2 µg/ml was above the desired minimum of 40%. Hence, the formulation can be therapeutically effective against a majority of strains of microorganisms indicated for treatment with amoxicillin.

5. Patent Status

PCT applications filed : WO 2005/065685, WO 2005/065641

6. Development Status

Phase I