**INTRODUCTION**

WCK 4873 (INN: Nafithromycin) is a novel Lactone-ketolide antibiotic developed (Wockhardt, India) as both oral and intravenous formulations for the treatment of Community Acquired Bacterial Pneumonia (CABP). It shows promising antibacterial activities against a wide range of pathogens causing CABP including Telithromycin (TEL)-resistant strains of *Streptococcus pneumoniae*, which also holds high potential against *S. aureus* and *S. pyogenes*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus mitis* and other oral and upper respiratory pathogens. Oral and intravenous Phase I pharmacokinetic studies of Nafithromycin have shown broad-spectrum and excellent bioavailability attributes in vitro in addition to encouraging tolerability and safety profile as observed in single ascending and multiple ascending dose studies. Many of the members of the macrolide/ketolide class of antibiotics have been widely recognized for their potential CYP inhibition assay. The reactions were initiated by addition of a co-factor NADPH and were terminated at different time points. The reactions were initiated by addition of a co-factor NADPH and were terminated at different time points.

**RESULTS AND DISCUSSION**

Nafithromycin along with SOL, CET, and TEL and reference positive inhibitors were evaluated as per FDA/EMEA guidelines by LC MS/MS method. CYP isoform specific inhibitory effect was further investigated by IC50 shift approach. Different concentrations of ketolides and reference positive and negative inhibitors were employed around Km: CYP1A2 (Phenacetin O-dealkylation), CYP2B6 (Bupropion hydroxylation), CYP2C8 (Amodiaquine N-Deethylation), CYP2C9 (Diclofenac 4-hydroxylation), CYP2C19 (Mephenytoin 4- hydroxylation), CYP2D6 (Dextromethorphan demethylation), CYP3A4 (midazolam 1-hydroxylation), CYP3A5 (S- Mephenytoin), CYP3A4/5 (Testosterone 6-α-hydroxylation), CYP3A4/5 (midazolam 1-hydroxylation), and CYP3A4/5 (Testosterone 6-α-hydroxylation).

1. **CYP1A2**
   - Dextromethorphan demethylation
   - N-Desmethyl metabolite of Nafithromycin which constitutes about 10% of the compound
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

2. **CYP2B6**
   - Bupropion hydroxylation
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

3. **CYP2C8**
   - Amodiaquine N-Deethylation
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

4. **CYP2C9**
   - Diclofenac 4-hydroxylation
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

5. **CYP2C19**
   - Mephenytoin 4- hydroxylation
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

6. **CYP2D6**
   - Dextromethorphan demethylation
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

7. **CYP2C19**
   - S- Mephenytoin
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

8. **CYP3A4**
   - 1-hydroxylation
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

9. **CYP3A5**
   - S- Mephenytoin
   - Metabolite based inhibition associated with them
   - Metabolite based inhibition associated with them

10. **CYP3A4**
    - 1-hydroxylation
    - Metabolite based inhibition associated with them
    - Metabolite based inhibition associated with them

**DISCLOSURES**

Note: Verapamil was used as a reference inhibitor.

**REFERENCES**

4. JS Satav. et al., ASM Microbe, 2016.