Clinical Pharmacology Perspectives on the Antiviral Activity of Azithromycin and Use in COVID-19.

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- Azithromycin is a broad-spectrum macrolide antibiotic with a long half-life and a large volume of distribution. It also exhibits anti-inflammatory activity.
- **Potential mechanism of antiviral activity of azithromycin:**
  1. Endosome maturation and function require an acidic environment. Azithromycin is a weak base and preferentially accumulates intracellularly in endosomal vesicles and lysosomes, which could increase pH levels, and potentially block endocytosis and/or viral genetic shedding from lysosomes, thereby limiting viral replication.
  2. Azithromycin may interfere with viral entry via binding between the SARS-CoV-2 spike protein and host receptor ACE2 (angiotensin converting enzyme-2).
  3. Azithromycin may amplify the host's interferon (IFN) pathway-mediated antiviral responses which lead to a reduction of viral replication.

The in vitro evidence suggest that azithromycin has antiviral properties, including activity against SARS-CoV-2, at concentrations that are physiologically achievable with doses used to treat bacterial infections in the lung.