

## **Supplementary Information**

# **A Systematic Review on the Clinical Pharmacokinetics of Cephalexin in Healthy and Diseased Populations**

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**Supplementary Table S1: Screening of articles based on title, abstract, presence of animals and language**

Sr. No.	Title of Article	Exclusion basis
1	(1971). "Cephalexin (Keflex)." Med Lett Drugs Ther 13(7): 25-26.	Abstract
2	(1991). "Swedish Study Group. A randomized multicenter trial to compare the influence of cefaclor and amoxycillin on the colonization resistance of the digestive tract in patients with lower respiratory tract infection." Infection 19(4): 208-215.	Title
3	(2000). "Antimicrobial treatment guidelines for acute bacterial rhinosinusitis: Sinus and Allergy Health Partnership *." Otolaryngology - Head and Neck Surgery 123(1, Part 2): S4-S31.	Title
4	(2001). "Antimicrobial treatment guidelines for acute bacterial rhinosinusitis." Disease-a-Month 47(11): 537-585.	Title
5	(2004). Chapter 4 Mechanisms of immunotoxic effects. Immunotoxicology of Drugs and Chemicals: an Experimental and Clinical Approach. J. Descotes, Elsevier. 1: 127-162.	Title
6	(2010). Oral Drug Absorption: Prediction And Assessment	Title
7	(2012). "APhA2012 abstracts of contributed papers." Journal of the American Pharmacists Association 52(2): 200-284.	Title
8	(2021). "Abstracts from the North American Neuromodulation Society's 2021 Virtual Meeting, January 15–16, 2021." Neuromodulation: Technology at the Neural Interface 24(4): e1-e276.	Title
9	Abduljalil, K. M. A. (2010). Advanced population pharmacokinetic modelling to quantify selected characteristics of drugs, Universitäts- und Landesbibliothek Bonn.	Title
10	Abdulwahab, H. G., et al. (2020). "Novel thiobarbiturates as potent urease inhibitors with potential antibacterial activity: Design, synthesis, radiolabeling and biodistribution study." Bioorg Med Chem 28(23): 115759.	Title
11	Actor, P., et al. (1976). "Cefatrizine (SK&F 60771), a new oral cephalosporin: serum levels and urinary recovery in humans after oral or intramuscular administration; comparative study with cephalexin and cefazolin." Antimicrobagents chemother 9(5): 800-803.	Abstract
12	Adam, D., et al. (1978). "Interference of the tissue concentration of antibiotics with a salidiuretic. Behaviour of cephadrine and cephalothin in brain tissue after additional administration of furosemide (author's transl)." Klinische Wochenschrift 56(5): 247-251.	Title
13	Agatonovic-Kustrin, S., et al. (2002). "Molecular descriptors that influence the amount of drugs transfer into human breast milk." J Pharm Biomed Anal 29(1): 103-119.	Title

14	Agoram, B., et al. (2001). "Predicting the impact of physiological and biochemical processes on oral drug bioavailability." Advanced Drug Delivery Reviews 50: S41-S67.	Title
15	Ahmadi, S., et al. (2016). "Comparison of single dose of cefazolion versus single dose of cefazolin plus seven days cephalexin prophylactic therapy in postoperative infections after elective cesarean section and immediate adverse effect of antibiotic on infants." Iranian journal of obstetrics, gynecology and infertility 19(15): 1-7.	Abstract
16	Ahrens, T. and K. G. Naber (1983). "Activity of cefroxadine and cephalexin in urinary tract infections: a double-blind comparative study." Infection 11(1): 25-30.	Abstract
17	Akimoto, Y., et al. (1998). "Cefaclor concentration in radicular granuloma after a single oral administration." Gen Pharmacol 31(2): 283-285.	Title
18	Akimoto, Y., et al. (1994). "Cefadroxil concentrations in human serum, gingiva, and mandibular bone following a single oral administration." J Oral Maxillofac Surg 52(4): 397-400; discussion 400-391.	Title
19	Akimoto, Y., et al. (1992). "Cefaclor concentrations in human serum, gingiva, mandibular bone, and dental follicle following a single oral administration." Gen Pharmacol 23(4): 639-642.	Title
20	Akimoto, Y., et al. (1996). "Cefaclor concentration in pus from abscess caused by odontogenic infection after a single oral administration." Gen Pharmacol 27(1): 177-179.	Title
21	Ali, I., et al. (2023). "Advancement in oral pharmacokinetics of an antibiotic Cefixime using amphiphilic 4-armed macrocyclic surfactant based niosomes." Arabian Journal of Chemistry 16(8): 104958.	Title
22	Allen, J. G. and L. J. Lees (1980). "Pharmacokinetics of alafosfalin, alone and in combination with cephalexin, in humans." Antimicrob Agents Chemother 17(6): 973-979.	Abstract
23	Altergott, C., et al. (2008). "Pediatric fingertip injuries: do prophylactic antibiotics alter infection rates?" Pediatric emergency care 24(3): 148-152.	Title
24	Aman, S. F., et al. (2010). "Studies of food drug interactions." Pak J Pharm Sci 23.	Title
25	Amidon, G. L., et al. (1988). "Estimating human oral fraction dose absorbed: a correlation using rat intestinal membrane permeability for passive and carrier-mediated compounds." Pharm Res 5(10): 651-654.	Animal
26	Anand, B. S., et al. (2004). "Pharmacokinetics of novel dipeptide ester prodrugs of acyclovir after oral administration: intestinal absorption and liver metabolism." Journal of Pharmacology Experimental Therapeutics 311(2): 659-667.	Title

27	Anand, B. S., et al. (2003). "Interactions of the dipeptide ester prodrugs of acyclovir with the intestinal oligopeptide transporter: competitive inhibition of glycylsarcosine transport in human intestinal cell line-Caco-2." <i>J Pharmacol Exp Ther</i> 304(2): 781-791.	Title
28	Andersson, K. E. (1978). "On the pharmacokinetics of cephalosporin antibiotics." <i>Scand J Infect Dis Suppl</i> (13): 37-46.	Abstract
29	Andreas, C. J., et al. (2017). "Mechanistic investigation of the negative food effect of modified release zolpidem." <i>European Journal of Pharmaceutical Sciences</i> 102: 284-298.	Title
30	Andriole, V. T. (1978). "Pharmacokinetics of cephalosporins in patients with normal or reduced renal function." <i>J Infect Dis</i> 137 Suppl: S88-s99.	Abstract
31	Arakawa, H., et al. (2016). "Possible interaction of quinolone antibiotics with peptide transporter 1 in oral absorption of peptide-mimetic drugs." <i>Biopharm Drug Dispos</i> 37(1): 39-45.	Title
32	Arakawa, H., et al. (2014). "Evaluation of a thiodipeptide, L-phenylalanyl-Ψ[CS-N]-L-alanine, as a novel probe for peptide transporter 1." <i>Drug Metab Pharmacokinet</i> 29(6): 470-474.	Title
33	Arakawa, S., et al. (1990). "A double-blind comparative study of S 6472 (a long-acting cefaclor) versus a conventional cefaclor preparation in complicated urinary tract infections." <i>Japanese journal of antibiotics</i> 43(11): 1873-1892.	Title
34	Arguello, F., et al. (1998). "Flavopiridol Induces Apoptosis of Normal Lymphoid Cells, Causes Immunosuppression, and Has Potent Antitumor Activity In Vivo Against Human Leukemia and Lymphoma Xenografts." <i>Blood</i> 91(7): 2482-2490.	Title
35	Avery, R. K. (2010). "Infectious Disease Following Kidney Transplant: Core Curriculum 2010." <i>American Journal of Kidney Diseases</i> 55(4): 755-771.	Title
36	Baba, S., et al. (1983). "The double-blind trial of cefroxadine and cephalexin in the treatment of acute suppurative otitis media and acute exacerbation of chronic suppurative otitis media." <i>Japanese journal of antibiotics</i> 36(9): 2595-2634.	Abstract
37	Bachmann, K., et al. (1986). "Impact of cefaclor on the pharmacokinetics of theophylline." <i>Ther Drug Monit</i> 8(2): 151-154.	Title
38	Badenoch, P. R., et al. (1986). "Effect of inflammation on antibiotic penetration into the anterior segment of the rat eye." <i>Invest Ophthalmol Vis Sci</i> 27(6): 958-965.	Animal
39	Badhan, R. K. S., et al. (2014). "Development of a physiologically-based pharmacokinetic model of the rat central nervous system." <i>Pharmaceutics</i> 6(1): 97-136.	Animal
40	Bailey, A., et al. (1970). "Cephalexin--a new oral antibiotic." <i>Practitioner</i> 205(230): 791-795.	Abstract

41	Ball, P., et al. (2004). "Safety profile of oral and intravenous moxifloxacin: Cumulative data from clinical trials and postmarketing studies." <i>Clin Ther</i> 26(7): 940-950.	Title
42	Ballantyne, F. N. (1985). "Comparative efficacy of cefadroxil and cefaclor in the treatment of skin and soft-tissue infections." <i>Clin Ther</i> 7(4): 487-491.	Title
43	Bamfo, N. O., et al. (2021). "Examination of urinary excretion of unchanged drug in humans and preclinical animal models: increasing the predictability of poor metabolism in humans." <i>Pharm Res</i> 38: 1139-1156.	Title
44	Bandak, S. I., et al. (1999). "Cefaclor af versus amoxycillin/clavulanate in acute bacterial exacerbations of chronic bronchitis: a randomised multicentre study." <i>Int J Clin Pract</i> 53(8): 578-583.	Title
45	Barberán, J., et al. (2007). "Update on osteo-articular infections and severe skin and soft tissue infections." <i>Enfermedades Infecciosas y Microbiología Clínica</i> 25: 28-36.	Title
46	Barbhaiya, R. H., et al. (1990). "Comparison of the effects of food on the pharmacokinetics of cefprozil and cefaclor." <i>Antimicrob Agents Chemother</i> 34(6): 1210-1213.	Title
47	Barbhaiya, R. H., et al. (1990). "Phase I study of multiple-dose cefprozil and comparison with cefaclor." <i>Antimicrob Agents Chemother</i> 34(6): 1198-1203.	Title
48	Barbhaiya, R. H., et al. (1990). "Comparison of cefprozil and cefaclor pharmacokinetics and tissue penetration." <i>Antimicrob Agents Chemother</i> 34(6): 1204-1209.	Title
49	Barkworth, M. F., et al. (1991). "[The biological availability of cefadroxil given simultaneously with N-acetylcysteine]." <i>Arzneimittelforschung</i> 41(8): 839-843.	Title
50	Barreca, T., et al. (1984). "Therapeutic experience with cofosfolactamines: clinical and bacteriological results of two multicentre double-blind studies." <i>Drugs Exp Clin Res</i> 10(1): 55-62.	Title
51	Barrios, S., et al. (1975). "Bioavailability of cephalexin after intramuscular injection of its lysine salt." <i>J Pharm Pharmacol</i> 27(9): 711-712.	Abstract
52	Basha, M., et al. (2018). "A potential antibacterial wound dressing of cefadroxil chitosan nanoparticles in situ gel: Fabrication, in vitro optimization and in vivo evaluation." <i>Int J Pharm</i> 544(1): 129-140.	Title
53	Bathini, L., et al. (2019). "Clinical Outcomes of Failing to Dose-Reduce Cephalosporin Antibiotics in Older Adults with CKD." <i>Clin J Am Soc Nephrol</i> 14(2): 197-205.	Title

54	Bauer, P. and A. Windorfer (1981). "[Cefadroxil - fewer single administrations in better bioavailability]." ZFA (Stuttgart) 57(31): 2174-2177.	Title
55	Bedenic, B., et al. (2006). "Urinary bactericidal activity of oral antibiotics against common urinary tract pathogens in an ex vivo model." Chemotherapy 52(6): 293-297.	Title
56	Belousov, I., et al. (1998). "Selection of antibacterial therapy for treatment of infections in elderly patients." Antibiot Khimioter 43(10): 19-23.	Title
57	Bennett, P., et al. (1996). Monographs on individual drugs. Drugs and Human Lactation, Elsevier: 75-532.	Title
58	Bennett, W. M., et al. (1983). "Drug Prescribing in Renal Failure: Dosing Guidelines for Adults." American Journal of Kidney Diseases 3(3): 155-193.	Title
59	Bergan, T. (1980). "Pharmacokinetics of a new cephalosporin, CGP 9000 (cefroxadine), in healthy volunteers." Chemotherapy 26(4): 225-230.	Title
60	Bergan, T. (1987). "Pharmacokinetic properties of the cephalosporins." Drugs 34 Suppl 2: 89-104.	Abstract
61	Bergan, T., et al. (1983). "Relationship between pharmacokinetics and bioavailability of cefroxadine (CGP 9000) and renal function." Chemotherapy 29(3): 163-173.	Title
62	Bergan, T., et al. (1970). "Human pharmacokinetics of cephalexin." Pharmacology 4(5): 264-272.	Abstract
63	Bergogne-Berezin, E., et al. (1978). "Pharmacokinetic study of beta-lactam antibiotics in bronchial secretions." Scand J Infect Dis Suppl(14): 267-272.	Title
64	Berlizot, F., et al. (2000). "Chronic nifedipine dosing enhances cephalexin bioavailability and intestinal absorption in conscious rats." Drug Metab Dispos 28(11): 1267-1269.	Animal
65	Berlizot, F., et al. (2000). "alpha(2)-adrenergic receptors stimulate oligopeptide transport in a human intestinal cell line." J Pharmacol Exp Ther 294(2): 466-472.	Title
66	Bersani, C., et al. (1986). "[Pharmacokinetics of cofosfolactamines in subjects with impaired kidney function]." G Ital Chemioter 33(2-3): 121-128.	Title
67	Beumer, H. M. and J. Veldkamp (1982). "Oral cefaclor for treatment of bronchitis--a comparative double-blind study versus amoxycillin." Int J Clin Pharmacol Ther Toxicol 20(3): 113-117.	Title

68	Beyssac, E., et al. (1991). "Comparison of continuous, constant rate enteral tube feeding in supine patients to bolus food intake in ambulatory, healthy subjects regarding bioavailability of perorally administered cefroxadine." <i>Methods Find Exp Clin Pharmacol</i> 13(9): 637-642.	Title
69	Beyssac, E., et al. (1991). "Peroral absorption of cefroxadine in patients within the first day after severe trauma: comparison to cefroxadine pharmacokinetics in fasted, healthy volunteers." <i>Methods Find Exp Clin Pharmacol</i> 13(8): 565-572.	Title
70	Bhavnani, S. M., et al. (2004). "Pharmacokinetics, safety, and tolerability of ascending single intravenous doses of oritavancin administered to healthy human subjects." <i>Diagnostic microbiology infectious disease</i> 50(2): 95-102.	Title
71	Bhutani, U., et al. (2021). "Oral Drug Delivery: Conventional to Long Acting New-Age Designs." <i>European Journal of Pharmaceutics and Biopharmaceutics</i> 162: 23-42.	Title
72	Billig, H., et al. (1990). "The disposition of valpromide in rats and the isolated perfused rat liver." <i>Drug metabolism disposition</i> 18(2): 238-244.	Animal
73	Bins, J. W. and H. Mattie (1988). "Saturation of the tubular excretion of beta-lactam antibiotics." <i>Br J Clin Pharmacol</i> 25(1): 41-50.	Title
74	Bjerre, C., et al. (1996). "Bioavailability of the sedative propiomazine after nasal administration in rats." <i>Int J Pharm</i> 144(2): 217-224.	Animal
75	Blondeau, J. M. (2000). "A review of clinical trials with fluoroquinolones with an emphasis on new agents." <i>Expert opinion on investigational drugs</i> 9(2): 383-413.	Title
76	Blumer, J. L. (2005). "Evolution of a new drug formulation: the rationale for high-dose, short-course therapy with azithromycin." <i>Int J Antimicrob Agents</i> 26: S143-S147.	Title
77	Bolding, O. T. (1980). "Comparison of the efficacy and safety of cefadroxil and cephalexin in treating acute urinary tract infections in women." <i>Journal of international medical research</i> 8(Suppl. 1): 34-39.	Abstract
78	Boobis, A. R. and P. J. Lewis (1983). "Pharmacokinetics in pregnancy." <i>Clinical Pharmacology in Obstetrics</i> .	Title
79	Boothman, R., et al. (1973). "Absorption and excretion of cephalexin by the newborn infant." <i>Arch Dis Child</i> 48(2): 147-150.	Abstract
80	Bottaro, G., et al. (2012). "5 days Cefaclor vs. 10 days amoxicillin/clavulanate in the treatment of childhood streptococcal pharyngitis. Data from a randomized clinical trial." <i>Minerva pediatrica</i> 64(3): 341-346.	Title
81	Bottoni, P. and S. Caroli (2018). "Presence of residues and metabolites of pharmaceuticals in environmental compartments, food commodities and workplaces: A review spanning the three-year period 2014–2016." <i>Microchemical Journal</i> 136: 2-24.	Title

82	Bourdet, D. L. (2005). Novel mechanisms in the intestinal absorption of hydrophilic cationic drugs, The University of North Carolina at Chapel Hill.	Title
83	Bouza, E. and A. Burillo (2010). "Oritavancin: a novel lipoglycopeptide active against Gram-positive pathogens including multiresistant strains." <i>Int J Antimicrob Agents</i> 36(5): 401-407.	Title
84	Bradley, J. S. (2023). "What Is the Appropriate Dose, Route, and Duration of Antibiotic Therapy for Pediatric Acute Hematogenous Osteomyelitis (AHO)? I Wish I Knew." <i>J Pediatric Infect Dis Soc</i> 12(2): 61-63.	Title
85	Bradley, J. S., et al. (2019). "Safety and efficacy of oral and/or intravenous tedizolid phosphate (TZD) in adolescents with acute bacterial skin and skin structure tissue infections (ABSSSI)." <i>Open forum infectious diseases</i> 6: S230-S231.	Title
86	Bratlid, D. and T. Bergan (1976). "Displacement of albumin-bound antimicrobial agents by bilirubin." <i>Pharmacology</i> 14(5): 464-472.	Title
87	Bretschneider, B., et al. (1999). "Intestinal transport of beta-lactam antibiotics: analysis of the affinity at the H <sup>+</sup> /peptide symporter (PEPT1), the uptake into Caco-2 cell monolayers and the transepithelial flux." <i>Pharm Res</i> 16(1): 55-61.	Title
88	Brisson, A. M. and J. B. Fourtillan (1982). "Pharmacokinetic study of cefadroxil following single and repeated doses." <i>J Antimicrob Chemother</i> 10 Suppl B: 11-15.	Title
89	Brockmann, W. and M. Badr (2010). "Chronic Kidney Disease: Pharmacological considerations for the dentist." <i>The Journal of the American Dental Association</i> 141(11): 1330-1339.	Title
90	Brogard, J. M. and F. Comte (1982). "Pharmacokinetics of the new cephalosporins." <i>Antibiot Chemother</i> (1971) 31: 145-210.	Abstract
91	Brogard, J. M., et al. (1978). "Pharmacokinetics of cephalosporin antibiotics." <i>Antibiot Chemother</i> (1971) 25: 123-162.	Abstract
92	Brogden, R. N., et al. (1982). "Trimethoprim: a review of its antibacterial activity, pharmacokinetics and therapeutic use in urinary tract infections." <i>Drugs</i> 23(6): 405-430.	Title
93	Brooks, S. and A. R. Dent (1984). "Comparison of bone levels after intramuscular administration of cephradine ('Velosef') or flucloxacillin/ampicillin in hip replacement." <i>Pharmatherapeutica</i> 3(10): 642-649.	Title
94	Brumfitt, W. and J. M. Hamilton-Miller (1999). "Cefaclor into the millennium." <i>J Chemother</i> 11(3): 163-178.	Title
95	Bucko, A. D., et al. (2002). "Randomized, double-blind, multicenter comparison of oral cefditoren 200 or 400 mg BID with either cefuroxime 250 mg BID or cefadroxil 500 mg BID for the treatment of uncomplicated skin and skin-structure infections." <i>Clin Ther</i> 24(7): 1134-1147.	Title

96	Buckpitt, A. R. and M. R. Boyd (1980). "A sensitive method for determination of 5-fluorouracil and 5-fluoro-2'-deoxyuridine in human plasma by high-pressure liquid chromatography." <i>Analytical Biochemistry</i> 106(2): 432-437.	Title
97	Bundgaard, H. and G. J. Friis (1992). "Prodrugs of peptides. 16. Isocyclosporin A as a potential prodrug of cyclosporin A." <i>Int J Pharm</i> 82(1): 85-90.	Title
98	Bunke, C. M., et al. (1983). "Pharmacokinetics of common antibiotics used in continuous ambulatory peritoneal dialysis." <i>Am J Kidney Dis</i> 3(2): 114-117.	Title
99	Bustrack, J. A., et al. (1980). "A comparative pharmacokinetic and safety study of an investigational oral cephalosporin, RMI 19,592." <i>Current therapeutic research - clinical and experimental</i> 28(2): 208-217.	Abstract
100	Butcher, R. H., et al. (1972). "Blood and urine levels of cephalexin in patients with impaired renal function." <i>Med J Aust</i> 2(23): 1282-1284.	Abstract
101	Buur, A., et al. (1988). "Prodrugs of propranolol: hydrolysis and intramolecular aminolysis of various propranolol esters and an oxazolidin-2-one derivative." <i>Int J Pharm</i> 42(1): 51-60.	Title
102	Byun, S.-Y., et al. (2016). "Pharmacokinetic study of meropenem in healthy beagle dogs receiving intermittent hemodialysis." <i>Journal of Veterinary Pharmacology Therapeutics</i> 39(6): 560-565.	Animal
103	Cadorniga, R., et al. (1990). "Pharmacokinetics of cefroxadine after infusion to healthy volunteers." <i>Int J Clin Pharmacol Ther Toxicol</i> 28(10): 435-439.	Title
104	Cain, T. J., et al. (1987). "Bone levels of cephadrine and cefuroxime after intravenous administration in patients undergoing total hip replacement." <i>International orthopaedics</i> 11(1): 61-63.	Title
105	Campanacci, L., et al. (1975). "[Antibiotic therapy and renal insufficiency. Pharmacokinetics of pivampicillin, cephaloridin and streptomycin in chronic uremic patients undergoing conservative or hemodialytic treatment]." <i>Minerva Med</i> 66(68): 3547-3565.	Title
106	Campbell, D. B. (1997). Chirality and kinetics. <i>Pharmacochimistry Library</i> . F. Awouters and K. C. Waugh, Elsevier. 28: 45-60.	Title
107	Cappelletty, D. M. and M. J. Rybak (1996). "Bactericidal activities of cefprozil, penicillin, cefaclor, cefixime, and loracarbef against penicillin-susceptible and -resistant <i>Streptococcus pneumoniae</i> in an in vitro pharmacodynamic infection model." <i>Antimicrob Agents Chemother</i> 40(5): 1148-1152.	Title
108	Caramatti, C., et al. (1980). "[Clinical evaluation of use of combinations of beta-lactamases in anti-infective therapy]." <i>Ateneo Parmense Acta Biomed</i> 51(1): 57-66.	Title

109	Carli, S., et al. (1999). "Absorption kinetics and bioavailability of cephalexin in the dog after oral and intramuscular administration." <i>J Vet Pharmacol Ther</i> 22(5): 308-313.	Animal
110	Carr, R. A. (1995). "Pharmacokinetics of Sotalol enantiomers." <i>Clin Pharmacol.</i>	Title
111	Carsenti-Etesse, H., et al. (1998). "Pharmacokinetic parameters and killing rates in serum of volunteers receiving amoxicillin, cefadroxil or cefixime alone or associated with niflumic acid or paracetamol." <i>Eur J Drug Metab Pharmacokinet</i> 23(3): 357-366.	Title
112	Casewell, M. W. and S. G. Bragman (1987). "The in-vitro activity of cefadroxil, and the interpretation of disc-susceptibility testing." <i>J Antimicrob Chemother</i> 19(5): 597-603.	Title
113	Castro, M. (1986). "A comparative study of cefadroxil and co-trimoxazole in patients with lower respiratory tract infections." <i>Drugs</i> 32 Suppl 3: 50-56.	Title
114	Cattrall, J. W. S., et al. (2019). "A pharmacokinetic-pharmacodynamic assessment of oral antibiotics for pyelonephritis." <i>Eur J Clin Microbiol Infect Dis</i> 38(12): 2311-2321.	Title
115	Cayen, M. N. (1985). "Disposition, metabolism and pharmacokinetics of antihyperlipidemic agents in laboratory animals and man." <i>Pharmacology &amp; Therapeutics</i> 29(2): 157-204.	Title
116	Cazzola, M., et al. (2000). "Interrelationship between the pharmacokinetics and pharmacodynamics of cefaclor advanced formulation in patients with acute exacerbation of chronic bronchitis." <i>J Chemother</i> 12(3): 216-222.	Title
117	Chang, Q., et al. (2009). "Studies on the influence of esterase inhibitor to the pharmacokinetic profiles of oseltamivir and oseltamivir carboxylate in rats using an improved LC/MS/MS method." <i>Biomed Chromatogr</i> 23(8): 852-857.	Animal
118	Charles, B. and S. Chulavatnatol (1993). "Simple analysis of amoxycillin in plasma by high performance liquid chromatography with internal standardization and ultraviolet detection." <i>Biomed Chromatogr</i> 7(4): 204-207.	Title
119	Chavada, V. D., et al. (2020). "Citrate/melamine functionalized gold nanoparticles for concurrent determination of allopurinol and its major metabolite, oxypurinol in plasma and pharmaceuticals." <i>Journal of Industrial and Engineering Chemistry</i> 84: 141-149.	Title
120	Chen, J., et al. (2012). "Bioequivalence studies of 2 oral cefaclor capsule formulations in chinese healthy subjects." <i>Arzneimittelforschung</i> 62(3): 134-137.	Title
121	Chen, L. and X. Chen (2012). "Results of molecular docking as descriptors to predict human serum albumin binding affinity." <i>Journal of Molecular Graphics and Modelling</i> 33: 35-43.	Title

122	Chen, M. L. (1992). "An alternative approach for assessment of rate of absorption in bioequivalence studies." <i>Pharm Res</i> 9(11): 1380-1385.	Title
123	Chen, X. (2000). Pharmacokinetically guided chemotherapy for biliary tract infection, The Ohio State University.	Title
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357	Since up to 90% of a theophylline dose is biotransformed, drugs influencing microsomal enzyme systems in the liver may affect the elimination of theophylline. Other integrated mechanisms (e.g., hepatic uptake) may also be altered by concurrent administration of other drugs. Whatever the mechanism, the interaction may be sufficient to necessitate adjustment of the theophylline dosage, preferably guided by plasma theophylline determinations. Comedication with phenobarbitone may require an increase in theophylline dose by about 30% due to increased clearance resulting from enzyme induction. Similarly, with phenytoin and carbamazepine, a dose increase of about 40-50% may be required. In the case of rifampicin, isoniazid, or sulphapyrazone comedication, an increase in dose of theophylline by about 20-25% may be needed. On the other hand, other drugs decrease theophylline clearance, making a reduction in the dose of concurrent theophylline advisable; with usual doses of erythromycin, propranolol, and isoprenaline (isoproterenol), a reduction of about 25% is needed; with cimetidine and oral contraceptive by about 30% or more; and with triacetyloleandomycin (troleandomycin), by about 50%. In high doses, the xanthine oxidase inhibitor allopurinol can also retard theophylline elimination, and a reduction of the theophylline dose by about 20% may be advisable. Conflicting results have been reported on the influence of frusemide (furosemide) and influenza vaccines, while data regarding the effect of corticosteroids, benzodiazepines, and verapamil on theophylline kinetics are not yet conclusive. Many drugs, however, appear not to significantly affect theophylline clearance. Some are from the same therapeutic group as the drugs mentioned above and offer clinical alternatives for coadministration with theophylline. Examples of drugs not found to have a significant effect on theophylline pharmacokinetics are ranitidine, josamycin, midecamycin, amoxycillin, tetracycline, cephalexin, cefaclor, orciprenaline, metoprolol, antacids, medroxyprogesterone acetate, metoclopramide, and metronidazole. Most of the drugs discussed in this review appear to not affect the volume of distribution of theophylline significantly.	Title
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855	Zhao, M., et al. (2016). "Animal models in the pharmacokinetic/pharmacodynamic evaluation of antimicrobial agents." <i>Bioorg Med Chem</i> 24(24): 6390-6400.	Animal
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**Supplementary Table S2: Quality assessment of included articles by Jadad scoring**

Sr. No.	Reference	JADAD Questions					JADAD score
		Was the study described as randomized?	Was the method used to generate the sequence of randomization described and appropriate?	Was the study described as double blind?	Was the method of double blinding described and appropriate?	Was there a description of withdrawals and dropouts?	
1-	Liew et. al	1	1	0	0	1	3
2-	Liu R et. al	1	1	0	0	1	3
3-	Hassanzadeh et. al	1	1	1	1	0	4
4-	Bataineh et. al	1	1	0	0	0	2
5-	Ding et. al	1	1	0	0	0	2
6-	Lecaillom et. al	0	0	0	0	0	0
7-	Ginsburg et. al	1	0	0	0	0	1
8-	Spyker et. al	0	0	0	0	0	0
9-	Nakagawa et. al	0	0	0	0	0	0
10-	Nahata et. al	0	0	0	0	0	0
11-	Lode et. al	1	1	0	0	0	2
12-	Evert et. al	1	1	0	0	0	2
13-	Kelly et. al	1	1	0	0	0	2
14-	Akimoto et. al	0	0	0	0	0	0
15-	Barbhayia et. al	1	1	0	0	0	2
16-	Finkelstein et. al	1	1	0	0	0	2
17-	Ding Y et. al	1	1	0	0	0	2

18-	Mohamed S et. al	1	1	0	0	0	2
19-	Welling et. al	1	1	0	0	0	2
20-	Bunke et. al	1	1	0	0	0	2
21-	Liu R et. al	1	1	0	0	0	2
22-	Regamey et. al	0	0	0	0	0	0
23-	Autmizguine et. Al	1	1	0	0	0	2

**Supplementary Table S3: Quality assessment of included articles by CACPK scoring**

	References																						
Questions	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Q1	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q2	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q3	Y	Y	Y	Y	Y	N	Y	N	Y	N	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	N	N
Q4	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q5	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q6	Y	Y	N	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N	Y	N	N
Q7	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q8	Y	Y	ID K	N	Y	N	ID K	ID K	N	Y	Y	N	Y	N	N	N	Y	Y	ID K	Y	Y	ID K	ID K
Q9	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q10	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q11	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q12	Y	ID K	ID K	ID K	N	N	ID K	N	N	N	ID K	N	ID K	ID K	N	N	N	N	N	N	N	N	N
Q13	Y	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q14	Y	Y	ID K	N	Y	N	N	N	N	Y	Y	Y	N	N	N	N	N	N	N	Y	Y	N	N
Q15	Y	Y	ID K	N	Y	ID K	N	N	N	Y	Y	Y	N	N	N	Y	N	N	Y	Y	N	N	
Q16	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Q17	N	N	N	N	N	N	N	N	N	Y	Y	Y	N	N	N	N	N	N	Y	Y	N	Y	Y

Q18	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	ID K	Y	N	Y	Y	Y	Y	N	Y	
Q19	Y	Y	Y	Y	Y	Y	Y	ID K	Y	Y	Y	ID K	Y	Y	ID K	Y	Y	Y	Y	Y	Y	
Q20	ID K	N	N	N	N	N	N	N	N	N	ID K	N	ID K									
Q21	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	ID K	Y	N	Y	Y	Y	Y	N	Y	
<b>DELPHI Score</b>	19	17	14	14	18	14	14	10	14	19	18	17	11	15	11	17	16	15	18	18	12	14

Y:Yes, N:No, IDK: I don't know

**Supplementary Table S4: Quality assessment of included articles by CASP scoring**

Reference	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate to address the aims of the research?	Was the research design appropriate to the aims of the research?	Are the study's theoretical underpinnings clear, concient and conceptually coherent?	Was the recruitment strategy appropriate to the aims of the search?	Was the data collected in a way that addresses the research issue?	Has the researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the analysis sufficient and rigorous?	Is there a clear statement of findings?	CASP Score
Liew et. al	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Liu R et. al	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Hassanzadeh et. al	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Bataineh et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Ding et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Lecailllom et. al	Y	N	N	Y	Y	Y	CT	N	Y	Y	6
Ginsburg et. al	Y	N	N	Y	Y	Y	N	Y	Y	Y	7
Spyker et. al	Y	N	N	Y	Y	Y	N	Y	Y	Y	7
Nakagawa et. al	Y	N	N	Y	N	Y	CT	N	Y	Y	5

Nahata et. al	Y	N	N	Y	Y	Y	N	Y	Y	Y	7
Lode et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Evert et. al	Y	Y	Y	Y	Y	Y	N	N	Y	Y	8
Kelly et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Akimoto et. al	Y	CT	CT	Y	Y	Y	CT	N	Y	Y	6
Barbhayia et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Finkelstein et. al	Y	Y	Y	Y	Y	Y	N	N	Y	Y	8
Ding Y et. al	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Mohamed S et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Welling et. al	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	9
Bunke et. al	Y	Y	Y	Y	Y	Y	N	N	Y	Y	8
Liu R et. al	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10
Regamey et. al	Y	CT	CT	Y	Y	Y	CT	CT	Y	Y	6
Autmizgui ne et. Al	Y	Y	N	Y	Y	Y	N	Y	Y	Y	8

Y:Yes, N:No, CT: Can't tell

**Supplementary Table S5: Risk of bias assessment of included articles by Cochrane Collaboration tool**

	Reference	Random sequence Generation (selection bias)	Allocation concealment (selection bias)	Blinding of participant and researchers (performed bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Bias Score
1-	Liew et. al	LR	LR	HR	UR	LR	LR	LR	5
2-	Liu R et. al	LR	LR	UR	UR	LR	LR	LR	5
3-	Hassanzadeh et. al	LR	LR	LR	LR	LR	LR	LR	7
4-	Bataineh et. al	LR	LR	HR	UR	UR	LR	LR	4
5-	Ding et. al	LR	LR	HR	UR	UR	LR	LR	4
6-	Lecaillom et. al	HR	HR	HR	UR	LR	LR	LR	3
7-	Ginsburg et. al	LR	LR	HR	HR	UR	LR	LR	4
8-	Spyker et. al	HR	HR	HR	UR	LR	LR	LR	3
9-	Nakagawa et. al	HR	HR	HR	UR	LR	LR	LR	3
10-	Nahata et. al	HR	HR	HR	UR	LR	LR	LR	3
11-	Lode et. al	LR	LR	HR	UR	LR	LR	LR	5
12-	Evert et. al	LR	LR	HR	HR	UR	LR	LR	4
13-	Kelly et. al	LR	LR	HR	HR	UR	LR	LR	4
14-	Akimoto et. al	HR	HR	HR	UR	LR	LR	LR	3
15-	Barbhayia et. al	LR	LR	HR	UR	LR	LR	LR	5
16-	Finkelstein et. al	HR	HR	HR	UR	LR	LR	LR	3
17-	Ding Y et. al	LR	LR	HR	UR	LR	LR	LR	5
18-	Mohamed S et. al	LR	LR	HR	UR	UR	LR	LR	4
19-	Welling et. al	LR	LR	HR	HR	UR	LR	LR	4

20-	Bunke et. al	HR	HR	HR	UR	LR	LR	LR	3
21-	Liu R et. al	HR	HR	HR	UR	LR	LR	LR	3
22-	Regamey et. al	HR	HR	HR	UR	LR	LR	LR	3
23-	Autmizguine et. Al	LR	LR	HR	HR	UR	LR	LR	4

LR: Low risk, HR: High risk, UR: Unclear risk