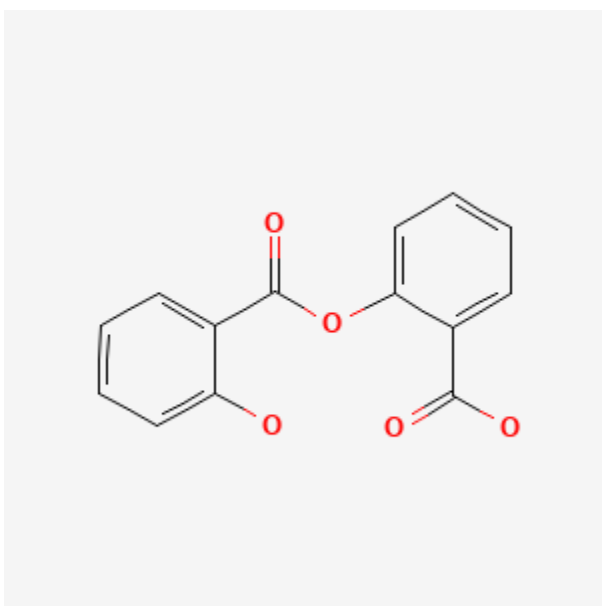




## Salsalate

Revised: August 16, 2021.

CASRN: 552-94-3



## Drug Levels and Effects

### Summary of Use during Lactation

Salsalate has not been studied during breastfeeding, but salsalate results in salicylic acid in the blood. Salicylic acid and aspirin have been studied during breastfeeding. The excretion of salicylate into breastmilk increases disproportionately as the maternal dosage increases. Long-term, high-dose maternal aspirin ingestion probably caused metabolic acidosis in one breastfed infant. Reye's syndrome is associated with aspirin administration to infants with viral infections, but the risk of Reye's syndrome from salicylate in breastmilk is unknown. An alternate drug is preferred over salsalate.

**Disclaimer:** Information presented in this database is not meant as a substitute for professional judgment. You should consult your healthcare provider for breastfeeding advice related to your particular situation. The U.S. government does not warrant or assume any liability or responsibility for the accuracy or completeness of the information on this Site.

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## Drug Levels

Milk levels have not been measured after maternal ingestion of salsalate, but have been measured after other salicylates, such as aspirin and sodium salicylate. All of these products result in salicylic acid in the blood and milk; however, some studies have not measured salicylate metabolites in breastmilk that may be hydrolyzed in the infant's gut and absorbed as salicylate.[1]

*Maternal Levels.* Milk and blood levels of the salicylate metabolites of aspirin were determined in 8 lactating women following oral administration of 1 gram of aspirin. Peak salicylic acid milk levels averaging 2.4 mg/L occurred 3 hours after the dose. Milk contents of salicyluric acid were greater than those of salicylic acid; a mean peak level of 10.2 mg/L was reached after 9 hours, and averaged 4.4 mg/L 24 hours after the dose. Total salicylate and metabolite levels were 5.1 mg/L at 3 hours, 9.9 mg/L at 6 hours, 11.2 mg/L at 9 hours and 10.2 mg/L at 12 hours after the dose. Acid labile conjugates were less than 0.2 mg/L.[2] Using an average salicylate plus salicylurate level over the first 12 hours, a fully breastfed infant would receive an average of 9.4% of the maternal weight-adjusted dosage.

Six nursing mothers who were 2 to 8 months postpartum (average 5 months) were given aspirin doses of 500, 1000 and 1500 mg of aspirin orally on 3 separate occasions. Peak breastmilk salicylate levels were 5.8 mg/L, 15.8 mg/L, and 38.8 mg/L, respectively. Salicylate metabolites were not measured. The time of the peak salicylate levels occurred between 2 and 6 hours after ingestion, with little variation in levels over time. The disproportionate increase in milk levels as the dose increased was attributed to nonlinear metabolism and protein binding.[3]

Two women given aspirin 454 mg orally had peak salicylate milk levels of about 1 mg/L 1 hour after the dose. The authors estimated that about 0.1% of the mothers' total dose would appear in breastmilk in 48 hours.[4] However, salicylate metabolites were not measured in milk.

A woman who was breastfeeding a 4-month-old was taking long-term aspirin therapy in dosages ranging from 2 to 5.9 grams daily. During this therapy, milk was obtained 4 hours after a 650 mg dose and just before taking a dose of 975 mg. The trough milk salicylate level was 2 mg/L and a peak level of 10 mg/L occurred 3 hours after the dose. Salicylate levels ranged from 4 to 7 mg/L over the 5 hours after the peak.[5] Using the peak level from this study, a fully breastfed infant would receive about 10% of the maternal weight-adjusted dosage of salicylate. The assay method used should have measured both salicylate and metabolites in milk.

*Infant Levels.* Four nursing mothers were given oral sodium salicylate in a dose of 20 mg/kg. Their exclusively breastfed infants ranged from 23 to 43 days of age. The infants' urine was collected until salicylate excretion was complete and found to contain 0.18 to 0.36% of the maternal dose, primarily as salicyluric acid.[1]

A 9-week-old infant who was born at 36 weeks gestation was receiving about 50% breastmilk and 50% formula. The infant's mother was taking 2.4 grams of aspirin daily and the infant's serum contained 65 mg/L of salicylate.[6]

## Effects in Breastfed Infants

A 16-day-old breastfed infant developed metabolic acidosis with a salicylate serum level of 240 mg/L and salicylate metabolites in the urine. The mother was taking 3.9 grams daily of aspirin for arthritis, and salicylate in breastmilk probably caused the infant's illness, but the possibility of direct administration to the infant could not be ruled out.[7]

Thrombocytopenia, fever, anorexia and petechiae occurred in a 5-month-old breastfed infant 5 days after her mother started taking aspirin for fever. One week after recovery, the infant was given a single dose of aspirin 125 mg and the platelet count dropped once again. The original symptoms were probably caused by salicylate in breastmilk.[8]

Hemolysis after aspirin and phenacetin taken by the mother of a 23-day-old, glucose-6-phosphate dehydrogenase (G6PD) deficient infant was possibly due to aspirin in breastmilk.[9]

In a telephone follow-up study, mothers reported no side effects among 15 infants exposed to aspirin (dose and infant age unspecified) in breastmilk.[10]

## Effects on Lactation and Breastmilk

Relevant published information was not found as of the revision date.

## Alternate Drugs to Consider

Acetaminophen, Ibuprofen

## References

1. Levy G. Salicylate pharmacokinetics in the human neonate. In, Morselli PL, Garattini S, Sereni F, eds. Basic and therapeutic aspects of perinatal pharmacology 1975;Raven Press :New York:319-30.
2. Pütter J, Satravaha P, Stockhausen H. Quantitative analysis of the main metabolites of acetylsalicylic acid. Comparative analysis in the blood and milk of lactating women. *Z Geburtshilfe Perinatol.* 1974;178:135–8. PubMed PMID: 4422623.
3. Jamali F, Keshavarz E. Salicylate excretion in breast milk. *Int J Pharm.* 1981;8:285–90. doi: [10.1016/0378-5173\(81\)90068-5](https://doi.org/10.1016/0378-5173(81)90068-5).
4. Findlay JW, DeAngelis RL, Kearney MF, et al. Analgesic drugs in breast milk and plasma. *Clin Pharmacol Ther.* 1981;29:625–33. PubMed PMID: 7214793.
5. Bailey DN, Welbert RT, Naylor A. A study of salicylate and caffeine excretion in the breast milk of two nursing mothers. *J Anal Toxicol.* 1982;6:64–8. PubMed PMID: 7098450.
6. Unsworth J, d'Assis-Fonseca A, Beswick DT. Serum salicylate levels in a breast fed infant. *Ann Rheum Dis.* 1987;46:638–9. PubMed PMID: 3662653.
7. Clark JH, Wilson WG. A. 16-day-old breast-fed infant with metabolic acidosis caused by salicylate. *Clin Pediatr (Phila).* 1981;20:53–4. PubMed PMID: 7449246.
8. Terragna A, Spirito L. *Minerva Pediatr.* 1967;19:613–6. [Thrombocytopenic purpura in an infant after administration of acetylsalicylic acid to the wet-nurse]. PubMed PMID: 6069440.
9. Harley JD, Robin H. "Late" neonatal jaundice in infants with glucose-6-phosphate dehydrogenase-deficient erythrocytes. *Australas Ann Med.* 1962;11:148–55. PubMed PMID: 13960788.
10. Ito S, Blajchman A, Stephenson M, et al. Prospective follow-up of adverse reactions in breast-fed infants exposed to maternal medication. *Am J Obstet Gynecol.* 1993;168:1393–9. PubMed PMID: 8498418.

## Substance Identification

### Substance Name

Salsalate

### CAS Registry Number

552-94-3

### Drug Class

Breast Feeding

Lactation

Analgesic Agents

Nonsteroidal Antiinflammatory Agents