Molecule ID: 54
Keyword: paracetamol
User Name: user4
Date of Creation: 2024-03-13 01:45:02

PubChem

Compound Name: Acetaminophen
Molecular Form: C8H9NO2, HOC6H4NHCOCH3
Molecular weight:151.16 g/mol
CAS registration: 103-90-2
ATC code: N - Nervous system / N02 - Analgesics / N02B - Other analgesics and antipyretics / N02BE - Anilides / N02BE01 - Paracetamol
IUPAC name: N-(4-hydroxyphenyl)acetamide
Solubility: 14 mg/mL at 25 °C
Physical description: Solid
Melting point: 170 °C
Decomposition: Decomposition not found
Half life: The half-life for adults is 2.5 h after an intravenous dose of 15 mg/kg. After an overdose, the half-life can range from 4 to 8 hours depending on the severity of injury to the liver, as it heavily metabolizes acetaminophen.
Reactivity: Reactivity not found

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Pharmacodynamics: URL: error Paragraphs: A. r. t. i. c. l. e. s. . n. o. t. . f. o. u. n. d

Overview of Efficacy: URL: error Paragraphs: A. r. t. i. c. l. e. s. . n. o. t. . f. o. u. n. d

Pharmacodynamics Drug Interaction: URL: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/7002186/ Paragraphs: 1 The rate of absorption of oral paracetamol depends on the rate of gastric emptying and is usually rapid and complete. The mean systemic availability is about 75%.. 2 Paracetamol is extensively metabolized and the plasma half-life is 1.5-2.5 hours. About 55% and 30% of a therapeutic dose is excreted in the urine as glucuronide and sulphate conjugates, respectively, whereas mercapturic acid and cysteine conjugates (representing conversion to a potentially toxic intermediate metabolite) each account for some 4% of the dose. Paracetamol metabolism is age- and dose-dependent.. 3 With hepatotoxic doses, paracetamol metabolism is impaired and the half-life prolonged. Sulphate conjugation is saturated and the proportion excreted as mercapturic acid and cysteine conjugates is increased.. 5 Phenacetin absorption depends on formulation. It is extensively metabolized to paracetamol and minor metabolites are probably responsible for toxicity

Clinical Studies: URL: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/29863746/ Paragraphs: Paracetamol (acetaminophen) is the most commonly used drug in the world, with a long record of use in acute and chronic pain. In recent years, the benefits of paracetamol use in chronic conditions has been questioned, notably in the areas of osteoarthritis and lower back pain. Over the same period, concerns over the long■term adverse effects of paracetamol use have increased, initially in the field of hypertension, but more recently in other areas as well. The evidence base for the adverse effects of chronic paracetamol use consists of many cohort and observational studies, with few randomized controlled trials, many of which contradict each other, so these studies must be interpreted with caution.. Unlike the closely related NSAIDs, paracetamol interferes with the peroxidase activity of COX isoenzymes, predominantly COX■2, particularly when the cellular environment is low in arachidonic

acid and peroxides 2, 19, 20. This explains paracetamol's apparent ‘central’ effect in earlier studies (as COX■2 is constitutively expressed in neural tissue) 19, 21, and why it appears to be ineffective in inflamed tissues (where peroxide and arachidonic acid are abundant), seen in conditions such as rheumatoid arthritis.. A proposed COX■3 isoenzyme (an exon splice variant of COX■1 seen in insects and rodents) has not been found in humans, and further studies suggest that paracetamol has no clinically significant effects on the COX■1 exon splice variants found so far in humans 19, 21. Other possible mechanisms of action include the inhibition of http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=2364 reuptake (and subsequent cannabinoid receptor http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=56 stimulation) by paracetamol metabolite N■arachidonoylphenolamine (AM404), which is produced by the conjugation of arachidonic acid and deacetylated paracetamol 22, and direct activation by this metabolite of the capsaicin receptor transient receptor potential cation channel subfamily V member 1 (http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=507) 23.. We conducted a literature search of PubMed, searching the years 1980 to 2016. An initial Pubmed review of ■paracetamol [Title] OR acetaminophen [Title]■ with ■side effects OR adverse effects■ revealed several key interest areas, which were subsequently searched for specifically as follows: we combined ■paracetamol [Title] OR acetaminophen [Title]■ with: ■hypertension OR blood pressure■; ■myocardial infarction OR cardiac OR cardiovascular■; ■stroke OR CVA OR cerebrovascular accident■; ■liver OR hepatic OR transaminase OR aminotransferase■; ■gastrointestinal OR bleeding OR anaemia■; ■renal OR kidney OR CKD OR chronic kidney disease■; ■respiratory OR asthma OR chest■; ■reproductive OR maternal OR ADHD OR attention deficit■. Papers were selected uisng the following criteria: (i) human subjects; and (ii) meta■analyses, reviews, RCTs, prospective studies and cohort studies.. Studies examining the effect of paracetamol on the incidence of cardiovascular disease are relatively sparse when compared to those on NSAIDs 27. Early studies focused on hypertension (which we have reviewed previously 28), owing to the known association of NSAIDs with hypertension, and the similar mechanism of action of paracetamol 29. One such study was a placebo■controlled crossover study of 20 treated hypertensive patients, in whom a 4 mmHg rise in blood pressure (BP) was found when paracetamol was administered 30.. However, observational and interventional studies examining the effect of paracetamol on hypertension have produced conflicting results 28. To date, most 32, 33, 34, but not all 35, 36, observational studies suggest that long■term paracetamol use increases the risk of developing hypertension. The Nurses' Health Study II, which included 80 020 participants, found that regular NSAID or paracetamol use was associated with an increased risk of developing hypertension 33: the relative risk (RR) of developing hypertension on NSAIDS was 1.86. [95% confidence interval (CI) 1.51 to 2.28) and on paracetamol was 2.00 (95% CI 1.52 to 2.62). It also seems that there is some evidence for a dose–response relationship between daily paracetamol dose and the risk of incident hypertension. This was observed not only in the Nurses’ Health Studies I and II 37, but also by Roberts et al. 6 for overall cardiovascular risk in their systematic review of paracetamol■related adverse effects.. By contrast, a retrospective observational study by Dawson et al. 36, with propensity matching, found no impact of paracetamol on BP in a cohort of 2754 participants with treated hypertension. Although observational studies may find an association between paracetamol use and hypertension, underlying confounders (such as chronic inflammatory conditions) need to be considered. Unfortunately, to date, interventional studies examining the impact of paracetamol on BP have been limited by study design and small sample size.. After aspirin was recognized to cause the rare but serious complication of Reye's syndrome, its use was banned in children under 12 years of age 40, 41. As aspirin use as an antipyretic waned in developed countries and paracetamol use became more common 42, concerns over paracetamol's association with asthma were raised 43. Observational and cross■sectional studies demonstrated a connection between paracetamol use and asthma diagnoses or exacerbations 44, 45, 46, 47, 48, 49, 50, 51. However, as for BP, almost all of these studies suffer from confounding by indication: recurrent symptomatic respiratory infections and febrile illnesses are more common in asthmatic patients and contribute to the onset of asthma in childhood 52, 53, 54.. In some studies, an increase in the risk/odds for developing asthma with increasing paracetamol use becomes nonsignificant when adjusted for recurrent

respiratory tract infection 55, 56, 57, although this is not universal 50. Meta■analyses of these observational studies tend to show only a small effect [e.g. odds ratio (OR) 1.15 for use in infancy], and suffer from considerable heterogeneity 44, 52.. Paracetamol may also cause an imbalance in lipoxygenase activity, brought about by COX inhibition, resulting in increased http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=272 and decreased http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=1883 production 60, 61, 65. This latter mechanism has support from studies carried out in patients with aspirin■associated asthma, in which decreases in forced expiratory volume in 1 s (FEV1) following paracetamol administration were observed 66.. Paracetamol has long been considered the 'safe' analgesic alternative to NSAIDs in patients prone to GI bleeding. Indeed, in studies of the analgesic effects of NSAIDS it is commonly used as a comparator, owing to the ethical issues of withholding analgesia 76, 77, 78. There is some evidence to support the safety of paracetamol. Examining adverse events reported in the Spanish drug monitoring system, Carvajal et al. 79 found that paracetamol use was associated with nausea (3.3% of all reported adverse events) and dyspepsia (4.2%), but not GI bleeding.. Furthermore, a meta■analysis of individual patient data from three case–control studies, looking at the risk of GI bleeding with individual NSAIDs, included paracetamol as a comparator and found no increased risk of GI bleeding with increasing daily doses of paracetamol 80.. However, recent epidemiological studies have identified a potential increased risk of upper GI bleeding with doses of paracetamol ≥2–3 g d–1. In 2001, a case–control study was conducted using the UK's General Practice Research Database (GPRD) 81. Adults aged 40–79 years with no history of prior GI disease or alcohol misuse (n = 13 605) were followed up between 1993 and 1998. The incidence of upper GI complications was documented, as was the prescription of paracetamol and potentially confounding medications.. The authors tried to compensate for this by excluding a history of Mallory–Weiss tear, cancer, oesophageal varices, coagulopathy or alcohol■related disease, and adjusting the RR for age, smoking, upper GI risk factors and concomitant medications, but this (they admitted) cannot exclude all bias. Additionally, the study was of prescriptions, not 'real■world' use. The authors had no data on OTC use of paracetamol by patients, and the daily dose was calculated from prescription frequencies, both of which have the potential to confound the results (although would not explain the apparent dose–response relationship found).. Early RCTs in this area appeared to give reassuring results. One crossover study examining the effects of 7 days of paracetamol, http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=4795 or placebo on endoscopic appearances found no acute effects of paracetamol on the GI mucosa 84. However, more recent RCTs have been less reassuring. In 2011, Doherty et al. 76 examined the effects of paracetamol (3 g d–1), ibuprofen (1200 mg d–1) and a combination of the two (ibuprofen 600 mg/paracetamol 1.5 g daily, or twice this dose) for chronic knee pain in a parallel■group RCT of 892 patients.. Based on these data, it seems that when taken regularly at doses of >2–3 g d–1 (i.e. at daily doses normally seen in chronic use), there is a significant risk of GI bleeding with paracetamol. The dose–response relationship seen in some of the studies would indicate that something in the mechanism of action of paracetamol can cause GI bleeding as an adverse effect, and that this effect is additive when combined with NSAIDs.. Over the past few decades, there have been several case reports and small studies implying a connection between the ingestion of therapeutic doses of paracetamol and liver injury 86. It has been known for many years that therapeutic paracetamol use (≤4 g d–1) has been associated with subclinical rises in liver injury markers 74. However, transient rises in alanine aminotransferase (ALT) can be secondary to many factors, such as exercise, vitamin intake, congestive heart failure, diabetes and medications such as aspirin, heparins and statins 87, 88.. Whether such an enzyme rise results in clinically significant liver injury is less clear. Heard et al. 89 looked at this issue with healthy volunteers in an RCT of long■term paracetamol ingestion (dose 4 g d–1). They found that ~50% of the paracetamol group experienced no ALT rise, ~25% had a transient rise, which was gone by day 16, and ~25% had ALT normalize by day 40 89. These findings are consistent with those from Dart and Bailey's review of observational data in >40 000 patients, showing a low incidence of transaminitis (0.4–1.0%) and no progression to hepatotoxicity 90.. This appeared to be supported by animal studies showing that CYP2E1 was induced by ethanol in rodents, and that levels of NAPQI and hepatotoxicity were increased when paracetamol was administered 86. However, researchers have failed to replicate

this finding in humans, and have found evidence of the opposite: CYP2E1 appears to increase only modestly with short■term alcohol use, reversing soon after abstinence 86, and one examination of cirrhotic livers found them to have 59% less CYP2E1 than control samples 92.. Children metabolize paracetamol differently to adults 100, and there is some concern that they may also suffer as a result of ingestion of therapeutic doses of paracetamol. This prompted Lavonas et al. 87 to perform a systematic review in 2010, examining 62 studies and >32 000 children receiving therapeutic■dose paracetamol (≤75 mg kg–1 d–1, up to a maximum of 4 g d–1) for an average of 3–5 days. The range of settings (inpatient, outpatient, primary care, developed and developing world) and indications for paracetamol (infective illness, postoperative pain) was comprehensive.. As the major active metabolite of phenacetin is paracetamol 109, some questioned whether chronic paracetamol use might also cause chronic kidney disease. In 1994, Perneger et al. 110 studied 716 subjects with end■stage renal disease (ESRD) and found that this was associated with an increase in paracetamol use in a dose■dependent fashion, with ~10% of the overall incidence of ESRD attributable to paracetamol use. The study unfortunately failed to adjust for possible previous use of phenacetin and NSAIDs, bringing its results into question.. However, large cohort studies have not found an association between maternal paracetamol use in the first trimester and either adverse pregnancy outcomes or congenital malformations 117, 118. Nevertheless, there is some evidence of increased risk with paracetamol use in pregnancy and neurodevelopmental disorders, respiratory illness and reproductive toxicity.. The association between paracetamol exposure in utero and the risk of long■term neurological disorders has been the focus of several controversial pharmaco■epidemiological studies. Brandlistuen et al. 119 suggested that maternal paracetamol use for >28 days during pregnancy was associated with problems in gross motor development, communication, externalizing and internalizing behaviour, and higher activity levels, when compared with controls. These data were obtained from a Norwegian sibling■controlled study (n = 2919) and based on parental reports of child behaviour at 18 months and 36 months.. Notably, these associations were stronger with increased frequency of paracetamol use and were not confounded by maternal inflammation or infection during pregnancy. Using hospital outcome coding data in the same patient cohort, the group later identified an association between prenatal paracetamol use and an increased risk of autistic spectrum disorder (ASD) accompanied by hyperkinetic symptoms (HR 1.51, 95% CI 1.19 to 1.92), but not with other ASD cases 121; other studies have suggested an association with ASD symptoms in male offspring only, with associations dependent on the frequency of exposure 122.. The mechanism by which paracetamol and its metabolites may affect neurological development is poorly understood. Animal studies have reported behavioural and cognitive changes in mice given paracetamol during neonatal brain development – specifically, locomotor activity and attainment of spatial learning 123. Levels of http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=4872 (BDNF) in the neonatal brain were affected (significantly increased in the frontal, and decreased in the parietal, cortices), postulating that this may be the mechanism of action.. In conclusion, on the basis of these studies, only weak associations between paracetamol exposure and neurodevelopmental issues have been identified, and no causal link can be inferred. The epidemiological studies that support a link are subject to confounding by unmeasured environmental factors, recall bias, diagnostic inaccuracy (most rely on coding data or parental recall for their outcomes) and differences in drop■out rates. Notably, few studies confirm the effect of duration and timing of paracetamol exposure, details that are critical in the assessment of toxicological risk in pregnancy.. The potential mechanisms by which paracetamol may contribute to the development/exacerbation of asthma have been described earlier. How paracetamol exposure in utero could cause asthma is less clear, unless glutathione levels are lowered sufficiently in the fetus to affect lung development. Some support for maternal intake of paracetamol affecting offspring comes from mouse studies, where adult mice exposed to paracetamol in utero underwent an allergic airway challenge 125. Increased airway infiltration by leukocytes (notably eosinophils) was observed, suggesting an increased susceptibility to asthma, but this finding has not been consistently reproduced 126.. The Avon Longitudinal Study of Parents and Children was one of the first epidemiological studies to examine the causal link between paracetamol exposure during pregnancy and childhood asthma 127. Frequent paracetamol use in late pregnancy (20–32 weeks) was associated with an increased risk of wheezing in the offspring at 30–42 months (adjusted OR 2.10, 95%

CI 1.30 to 3.41), particularly if wheezing started before 6 months (termed ‘persistent wheezers’ – OR 2.34, 95% CI 1.24 to 4.40). Two further cohort studies suggested that paracetamol use during any time of pregnancy was associated with a small increased risk of asthma or bronchitis among children at 18 months (RR 1.17, 95% CI 1.13 to 1.23) and 7 years (RR 1.15, 95% CI 1.02 to 1.29) 128, 129.. However, maternal infections, including respiratory infections, have already been associated with an increase in childhood asthma 130, 131. Paracetamol use may simply be a surrogate for these disease states. Notably, maternal paracetamol use for non■infectious disorders revealed no increased risk of wheezing in children 132. Further studies expanded on this theme of confounding by paracetamol indication and have highlighted that the increased risk of asthma diagnosis in children exposed to paracetamol prenatally (unadjusted OR 1.36, 95% CI 1.14 to 1.61) drops significantly (OR 1.26, 95% CI 1.02 to 1.58) when adjusted for potential confounders 133.. Several clinical studies associate paracetamol exposure during pregnancy with increased occurrence of cryptorchidism, particularly when used in for >2 weeks in the second trimester 136, 139, 140. Few of these studies considered indication for paracetamol use in their analyses, and, latterly, reanalysis of these data sets showed slightly lower HRs for paracetamol exposure during weeks 8–14 among women who did not report an illness that would trigger weak analgesic use 141. This is an interesting paradoxical observation, given that this time frame represents the human fetal programming window, disruption of which has previously been linked to reduced male infant ano–genital distance 135, 142.. However, we should also note that several large cohort studies have not identified any association between paracetamol and cryptorchidism 117, 143, 144, 145. Indeed, the use of paracetamol may decrease the risk of selected congenital abnormalities when used for febrile illness 144.. The continuing search for evidence that paracetamol causes harm in pregnancy clearly highlights the difficulty in implying causation from pharmaco■epidemiological studies. Extrapolation of preclinical toxicology data to humans may suggest associations with asthma, ADHD and androgen disruption but the small associations seen in clinical cohort studies may be explained by various confounders and biases inherent in the study designs. Confidently teasing apart these issues would require RCTs, which would be difficult to perform ethically in pregnant populations.. Carefully designed, long■term, sibling■ and sex■matched cohort studies are more ethically acceptable, and would further our understanding of the risks. While the evidence base is uncertain, care should be taken to avoid raising poorly founded concerns among pregnant women because of the risk of switching to other analgesic/antipyretic drugs with less favourable risk profiles 113. Untreated febrile illness is associated with severe harm to both mother and child, posing a far greater risk than that postulated for paracetamol exposure 130, 146, 147, 148.. Clearly, there remains considerable uncertainty regarding the chronic adverse effects of paracetamol use. The evidence base in each of the above sections relies mostly on observational and cohort studies, and so is prone to inherent biases. The positive associations found in these studies are generally weak, and often contradictory. Few RCTs have been performed but, when undertaken, usually give reassuring results. Further studies are required in many areas, but RCTs may be difficult to perform, either because they would need to be very large to detect the modest increases in risk seen in the observational studies, or because of the significant ethical issues of using placebo in patients in pain, as well as of conducting trials in children and pregnant women.. The present review is designed to provide an objective summary of the evidence base for chronic adverse effects of paracetamol use. We hope that by highlighting the key epidemiological studies, RCTs, meta■analyses and reviews, we have provided a valuable summary of knowledge in this field. We hope this work will help clinicians and their patients to make an evidence■based, informed decision regarding their chronic pain management, based on the likelihood of clinically relevant adverse effects.

Overview of Safety: URL: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/34208683/ Paragraphs: N-acetylcysteine (NAC) is a medicine widely used to treat paracetamol overdose and as a mucolytic compound. It has a well-established safety profile, and its toxicity is uncommon and dependent on the route of administration and high dosages. Its remarkable antioxidant and anti-inflammatory capacity is the biochemical basis used to treat several diseases related to oxidative stress and inflammation. The primary role of NAC as an antioxidant stems from its ability to increase the intracellular concentration of glutathione (GSH), which is the most crucial biothiol responsible for cellular redox imbalance.. The

primary role of NAC is associated with its antioxidant and anti-inflammatory activity, which favors the maintenance of a cellular redox imbalance. For this reason, its therapeutic potential concerns a series of diseases that link oxidative stress to its etiology and progression [3,4]. However, the mechanisms via which NAC exerts its antioxidant and cytoprotective capacity in different physiological conditions have not yet been fully clarified [5]. The growing interest in investigating the favorable effects of NAC involves not only its action as a potent cell bio-protector but also its pharmacokinetic characteristics, related to safety, absorption, and bioavailability, associated with its low cost [3,4].. The inhaled form of NAC is most commonly used to treat respiratory diseases. In general, studies with inhaled NAC demonstrated a safety profile similar to other formulations, demonstrating good tolerance to this type of formulation [25,26,27]. Adverse symptoms after administration of inhaled NAC include bacterial pneumonia, cough, sore throat, and drug-induced pneumonitis, among which coughing is the most common [27]. A systematic review with meta-analysis showed that the incidence of adverse effects was significantly higher in the treatment with inhaled NAC when compared to oral NAC; however, the study did not identify any significant difference in the incidence of adverse effects between NAC therapy and the treatments of control [28].. Typically, NAC is administered orally, using 600–1200 mg tablets up to three times a day [11]. For the treatment of chronic diseases such as COPD, which requires long-term use, the maximum licensed dose is 600 mg/day, but doses above 600 mg/day are constantly used in different clinical trials. The safety profile of NAC is usually similar, both for low doses (≤600 mg/day) and for high doses (>600 mg/day). Studies with a dosage up to 3000 mg/day in respiratory diseases have shown that NAC is safe and well tolerated [27] (Table 2).. Similarly, the placebo-controlled study on efficacy and safety of N-acetylcysteine high dose in exacerbations of chronic obstructive pulmonary disease held (PANTHEON) with 1006 patients with moderate and severe COPD, treated with 1200 mg of oral NAC per day, resulted in a significant reduction in acute exacerbations of COPD in the treated group compared to the placebo group, especially in patients with moderate disease [54].. There were no significant general differences in the change in forced vital capacity (FVC) between the groups. Changes in other parameters, such as changes in lower arterial oxygen saturation, 6 min walking distance test (6MWD), and abnormal pulmonary function parameters (PFT) also did not show significant differences between the NAC and control groups. Regarding the safety of inhaled NAC, there were no significant differences in the number of adverse events reported for both groups, demonstrating that, in general, NAC was well tolerated.. Rogliani et al. (2016) [62], in their systematic review and meta-analysis, analyzed the efficacy and safety of drugs frequently used in IPF, pirfenidone and nintedanib, in addition to NAC, in 3847 patients (2254 treated and 1593 placebo). The study showed that both pirfenidone and nintedanib, but not NAC, were significantly effective in reducing the progression of IPF. In addition, the study also d attention to the safety of NAC (concentrations of 704.8 mg/day inhaled at 1800 mg/day in tablet form), suggesting a higher risk of adverse events, despite insignificant results.. Another recent meta-analysis [28], which included 21 studies published between 2005 and 2016, assessed the efficacy and safety of NAC therapy in IPF. Of the 1354 patients, 695 received NAC alone orally or inhaled or combined with other medications (commonly corticosteroids and pirfenidone) and 659 received other therapies. The commonly used oral dose was 1800 mg per day and the inhalation dose was 704.8 mg. Analysis of the data showed that NAC can decrease the decline in lung function in patients with IPF, related to the reduction in the decline in forced vital capacity (FVC) and in the diffusion capacity of carbon monoxide (DLCO), with slow disease progression due to stabilizing arterial oxygen partial pressure (PaO2).. A multicenter trial [68] evaluated the safety and efficacy of oral supplementation of 2000 mg of NAC per day associated with treatment with antipsychotic medication and demonstrated moderate benefits for treatment with NAC, which reduced the clinical severity measured by the Clinical Global Impression (CGI) scale and the Positive and Negative Syndrome Scale (PANSS). Additionally, Sepehrmanesh et al. (2018) [69] showed that the administration of 1200 mg of NAC had a positive impact on the positive, negative, general, and total psychopathological symptoms analyzed by PANSS, along with an improvement of cognitive performance.. More recently, experts produced an updated evidence-based guide to help clinical practice in the face of episodes of paracetamol poisoning, which is the most common cause of severe acute liver injury in Western countries (Box 2). According to the new guidelines, two bags of NAC administered intravenously (200 mg/kg in 4 h, then 100 mg/kg in 16 h) has a similar efficacy to the

previous recommended dosage (of three bags), with the advantage of significantly reducing adverse reactions. The protocol also established a weight limit of 110 kg, with a maximum dosage of intravenous NAC equivalent to 22 g in the first infusion and 11 g in the second. However, as described in a systematic review, there is a lack of standards and details of the results of the few randomized clinical trials performed, which hinders the accuracy of information regarding the safety and efficacy of the applicability of NAC associated with the use of antibiotics in Helicobacter pylori-infected individuals [172]. Supporting the findings of this meta-analysis, a later study that aimed to assess the use of NAC associated with first-line triple therapy did not report an additive effect on the rate of eradication of the bacterium, when associated with the two therapeutic regimens [173].. Furthermore, evidence suggests that NAC supplementation, when performed correctly, may be able to improve distal intestinal obstruction syndrome, especially in older individuals; however, more studies need to be performed in order to assess dose, route of administration, and safety [176,177].. The same research group in a prospective double-blind study with 22 pregnant women with a clinical diagnosis of chorioamnionitis and 24 newborns (including two pairs of twins) sought to assess the safety of NAC in the pre- and postnatal maternal and child group. The study treated women before delivery with NAC (100 mg/kg/dose) or saline, administered intravenously every 6 h until birth. The newborns in the treated group received NAC (preterm: 12.5 mg/kg/dose; term: 25 mg/kg/dose) 6 h after the mother’s last dose and every 12 h for five doses.. Oxidative stress induces the expression of the stromal monocarboxylate transporter 4 (MCT4), a marker of catabolism frequently elevated in breast cancer, suggesting the transport of cancer-associated stromal catabolites to highly proliferative cancer cells. Therefore, as NAC tends to prefer cells with altered glucose, it is understood that cells with a high concentration of MCT4 would be more susceptible to the effects of the drug. Thus, a pilot study exposed that NAC expressed safety and biological activity in breast cancer, where it reduced the proliferation of cells and the expression of MCT4 [190].

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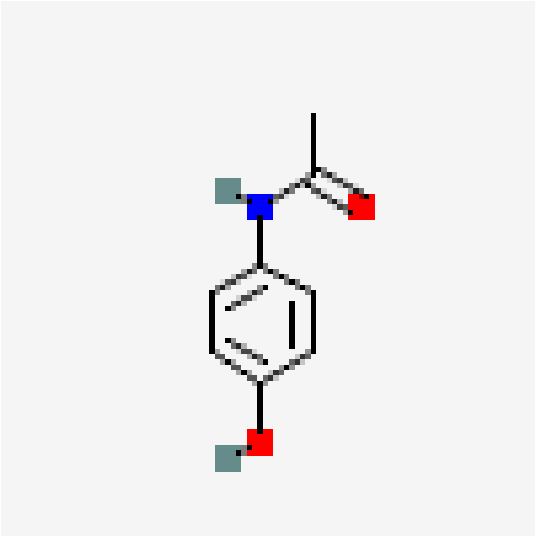
Benefits/Risks: URL: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/36268928/ Paragraphs: More than half of pregnant women are usually affected by odontogenic pain affects. Pain often accompanies periapical or pulp infections and increases the risks to pregnant patients and their fetuses. The American Dental Association, in partnership with the American College of Obstetricians and Gynecologists, has offered a strong declaration reaffirming the significance of suitable and timely oral health care as an indispensable constituent of a healthy pregnancy. However, there is lack of knowledge about the use of antibiotics in endodontic treatment.. Oral disease in pregnant women is a major public health issue worldwide.1 Pregnancy does come with inherent risks and the idea that dental treatment should not be implemented due to pregnancy is not debatable. Special concerns are necessary as a pregnant woman seeks dental care;2,3 hence, the treatment related to these patients may need more attention to reduce treatment time and make changes in the type of dental treatment and prescribed drugs.4 Appropriate risk assessment for the mother and fetus should be performed.3According to results of a novel study about pregnant women, it was recognized that more than 43% of them have oral health problems, containing odontogenic infections and pain.5. According to the obtained results of some studies in Canada and Netherlands, about 25% to 50% of pregnant women have received antibiotics.21,22 However, it is necessary to prescribe antibiotics to pregnant women after evaluating their disadvantages and advantages.23 It should also be noted that infections can be dangerous for both mother and fetus. For example, one of the risks of spreading infection from the mandibular second molars is the possibility of Ludwig's angina.24,25. Category D: Antibiotics that have side effects, but they have been proven in pregnancy, but when necessary, their benefits are more than their disadvantages.. Despite the low percentage of births less than 32 weeks' gestation (only 1% to 2% of all births), they are reason for 50% of long-term neurological problems as well as 60% of prenatal deaths.43,47 Pointing to the financial issues, preterm labor is remarkably significant as one-tenth of the cost of general child care and one-third of the cost of caring for infants is related to preterm labor.48,61During the two past decades, many kinds of investigations have underlined the reasons of preterm labor and consequently various correlated risk elements have been recognized.62

Most common reported ones are congenital causes of infectious origin.63-65 The possible associations between preterm labor and infection can be explained by models that claim that preterm labor is initiated by an inflammatory reaction to pro-inflammatory cytokines such as IL-6, IL-8, interleukin (IL). In conclusion, according to the results of researches, aspecifically evidences published by the American Dental Association with American Obstetricians, the use of some antibiotics during pregnancy are allowed and can be used normally and safely by pregnant women.



Img 1: Molecule structure of paracetamol (Source: PubChem)