Questions and Information for Students
Pharmaceutical Magnesium Compounds and Mixtures
By Dr. David Cash

1. Pharmaceutical Magnesium Ion from Magnesium Oxide or Magnesium Hydroxide

A. Magnesium Supplementation. Magnesium ion is an essential nutrient for humans (1), found in many foods. It is safely absorbed from the digestive tract. The simplest forms of magnesium ion used pharmaceutically are magnesium oxide, MgO, and its close relative magnesium hydroxide, $Mg(OH)_2$. These salts are both alkaline substances. For low-dosage supplements, either compound may be placed in a capsule for ingestion by swallowing. When the contents are released in the stomach, the magnesium salt reacts immediately with hydrochloric acid in the stomach to form aqueous magnesium ion for absorption.

Useful Information: **MgO = 40.31 g/mol** **$Mg(OH)_2$ = 58.32 g/mol**

1. Calculate and fill in the values of percent by mass of magnesium in each of the salts in the table.

Formula	**MgO**	**$Mg(OH)_2$**
Percent by Mass Mg		

2. Calculate the required amount in mg units of each of the two compounds needed in a capsule to provide 150 mg of magnesium ion.

3 Write a balanced chemical equation for the reaction of each solid compound with aqueous hydrochloric acid in the stomach to form aqueous magnesium ion.

4. Calculate the amount in millimoles of hydrochloric acid required to dissolve the calculated amount of each compound. Why are these amounts equal?

B. Magnesium Laxatives. When magnesium oxide (magnesia) MgO, is added to water, an immediate reaction produces a fine precipitate of a white solid, magnesium hydroxide, $Mg(OH)_2$. The resulting milky suspension is called milk of magnesia. This suspension has long been used as a laxative. A popular brand of Milk of Magnesia (2) has the following directions: Stir well. Each mL of suspension contains 80 mg of magnesium, Adult Dose 2 to 4 tablespoonfuls, 30 to 60 mL.
(One Tablespoonful = 15 mL)

Magnesium ion is an essential nutrient for humans. How then can it also be a laxative? Magnesium ion absorbance from the digestive tract is limited to an amount in the same order of magnitude as the daily nutritional requirement. The laxative dosage is nearly ten times as much as the nutritional requirement. The unabsorbed magnesium ions of the laxative dose and their counter anions reach the colon, where they exert an osmotic laxative effect (3).

5. Calculate the mass of magnesium in the lower and upper dosage of Milk of Magnesia. Answer in mg units.

Volume of Milk of Magnesia	**30 mL**	**60 mL**
Mass Mg		

2. Pharmaceutical Magnesium Ion Supplementation from Magnesium Citrate

Magnesium citrate, called magnesium citrate 3:2 by Wikipedia (4) has the formula and molar mass given below. Magnesium citrate is soluble in water. It occurs in the solid state as an anhydrous salt, or as a hydrate salt with 3 to 14 moles of water per mole. It is available commercially as mixtures of crystals of the anhydrous salt, the nonahydrate (9-hydrate) and the 14-hydrate.

Required Information

Citric Acid (a triprotic acid)
$C_6H_8O_7$ or $H_3C_6H_5O_7$ = 192.1 g/mol
Magnesium Citrate $Mg_3(C_6H_5O_7)_2$ = 451.1 g/mol

6. Magnesium oxide solid reacts with dissolved citric acid forming soluble magnesium citrate. Write a balanced chemical equation including physical states for this reaction.

7. Calculate and fill in the values of molar mass and percent by mass of magnesium for each of the crystalline salts in the table.

Formula	**$Mg_3(C_6H_5O_7)_2$**	**$Mg_3(C_6H_5O_7)_2.9H_2O$**	**$Mg_3(C_6H_5O_7)_2.14H_2O$**
Molar Mass			
Percent by Mass Mg			

8. Manufacturers of magnesium citrate produce batches which are mixtures of the crystalline salts in Question 7. Different manufacturers use different conditions of synthesis, so their products are not identical. Use the given equations to solve for the missing values.

Supplier / Batch	Percent by Mass Magnesium	Average Molar Mass	Average Value of X
Supplier 1 (5) / Batch 1	**11.5 %**		
Supplier 2 (6) / Batch 2	**14.5 %**		

$$\frac{\textbf{3} \times \textbf{Molar Mass of Magnesium}}{\textbf{Average Molar Mass of Batch}} \times 100\ \% = \text{Percent by Mass Magnesium}$$

Average Molar Mass of Batch = [451.1 + x*(18.0)] g/mol
(Where x is the Average Value)

3. Using Magnesium Citrate in Low-Dose Magnesium Supplement Products

Image - D. Cash 2025

Magnesium citrate, called magnesium citrate (3:2) by Wikipedia (4), is an ionic salt. It is relatively soluble in water and slightly hygroscopic (7). It is difficult to produce commercially with a precise magnesium content, and difficult to use in manufacturing of pharmaceuticals without mixing with processing additives. It is difficult to keep dry in storage. It is used by the manufacturers of fixed low-dosage magnesium supplements by the addition of processing aids such as micro-crystalline cellulose (MCC) (8). This tactic allows the manufacturer to produce tablets or capsules which are swallowed whole, reducing the storage issues.

Webber Naturals Magnesium Citrate -
Bottle Label Information:
Each capsule contains magnesium (as citrate) 150 mg.
Nonmedicinal ingredients: microcrystalline cellulose, vegetable grade magnesium stearate (lubricant).

9. Calculate the mass of magnesium citrate required in a capsule containing 150 mg of magnesium.

4. Introduction to Reactive Mixture Magnesium Citrate Laxatives

The additive MCC used in magnesium citrate supplements is insoluble in water and hydrophobic. Using such a mixture for a high dosage laxative product would not be commercially acceptable, since the powder mixture cannot be kept dry in storage, would lump and would not flow well from its package into a glass of water for dissolution and ingestion, and would not fully dissolve.
The consumer would not readily accept such a product.

The manufacturers of magnesium citrate laxatives have overcome this obstacle. The active ingredient of a magnesium citrate laxative pharmaceutical is not magnesium citrate but rather a dried powder mixture of anhydrous citric acid and a basic magnesium salt. Dissolving in water allows chemical reaction(s) to occur and results in an aqueous solution of magnesium citrate which is then ingested.

Two basic (alkaline) magnesium salts are used. The first is magnesium oxide, MgO, in a form known commercially as light magnesium oxide. The second is a magnesium hydroxy carbonate known commercially as heavy magnesium carbonate, $Mg_5(CO_3)_4(OH)_2.5\,H_2O$. Light magnesium oxide and heavy magnesium carbonate are described more fully in Sections 7 and 8 below.

There are two reaction types to consider:

A. Light magnesium oxide mixed with anhydrous citric acid.

B. Heavy magnesium carbonate mixed with anhydrous citric acid.

5. Light Magnesium Oxide / Anhydrous Citric Acid Mixtures

Ferring Pharmaceuticals of Switzerland manufactures this formulation and sells it around the world under at least four trademarked names: as Picolax® (in Europe), as Pico-Salax® (in Canada), as Picosalax® (in Australia), and as Prepopik® (in the U.S.) The formulation information available for Picolax is the most complete (9, 10).

Image D. Cash 2022

Formulation

Each sachet contains the following active ingredients:

Sodium picosulfate	10.0 mg
Magnesium oxide, light	3.5 g
Citric acid, anhydrous	12.0 g

Each sachet also contains:

Potassium hydrogen carbonate	0.5 g

[equivalent to 5 mmol (195 mg) potassium]
Sodium saccharin
Natural spray-dried orange flavour which contains acacia gum, lactose, ascorbic acid, butylated hydroxyanisole or cranberry flavor which contains maltodextrin, glyceryl triacetate (triacetin) and sodium octenyl succinated starch.

Chemical Reactions

Four chemical reactions occur when a dosage of this powder is dissolved in water solution. One dosage is used for a laxative effect, two doses for a purgative effect.
You can view the dissolution process in a YouTube video (11).
Both the absolute amount of each substance present and the relative amounts are important in ensuring the safety and efficacy of the pharmaceutical.

In this question set, for writing equations and calculating yields, magnesium citrate will be taken to have the formula $Mg_3(C_6H_5O_7)_2$. This is a convenient assumption. It will be called magnesium citrate, not either of the common names trimagnesium citrate or magnesium citrate 3:2 used by Wikipedia.

Required Information

Citric Acid (a triprotic acid)
$C_6H_8O_7$ or $H_3C_6H_5O_7$ = 192.1 g/mol
Magnesium Oxide MgO = 40.31 g/mol
Magnesium Citrate $Mg_3(C_6H_5O_7)_2$ = 451.1 g/mol
Potassium Bicarbonate $KHCO_3$ = 100.1 g/mol

Chemical Reactions

10. Solid magnesium oxide (magnesia) reacts immediately with water to form a slurry of insoluble magnesium hydroxide (milk of magnesia). This product is observed as a milky precipitate.
    Write a balanced chemical equation including physical states for this reaction.
    This is **Equation 1.**

11. Soluble citric acid dissolves in water reacting with the solid magnesium hydroxide which has precipitated to form soluble magnesium citrate.
    Write a balanced chemical equation including physical states for this reaction.
    Use the formula $H_3C_6H_5O_7$ for the citric acid to emphasize that citric acid is a triprotic acid having three ionizable hydrogen atoms. This is **Equation 2.**

12. Solid magnesium oxide also reacts directly with dissolved citric acid forming soluble magnesium citrate. Write a balanced chemical equation including physical states for this reaction. This is **Equation 3.**

    Notice that Equation 3 = (3 × Equation 1) + Equation 2

    Chemical equations are additive.
    Equation 3 is the overall equation to be used for quantity calculations.

    Note: Equations are added together by writing down all the left-side reagents with coefficients to the left of the arrow, then writing down all the right-side reagents with coefficients to the right of the arrow. Then if any reagents are present on both sides, a subtraction is made to remove the lesser amount from both sides.

    Example: …….+ 3 H_2O + ……. → …….+ 5 H_2O + ……

    Becomes: ………….. → …….+ 2 H_2O + ……

13. The dissolved citric acid also reacts with the potassium hydrogen carbonate (potassium bicarbonate), which is very soluble in water. Carbon dioxide gas is produced.
    Write a balanced chemical equation including physical states for this reaction. This is **Equation 4.**

    This reaction produces effervescence due to the production of carbon dioxide gas and produces dissolved potassium ion. The effervescence improves the taste of the ingested medicine, and the potassium ion is useful. When absorbed it will replace the potassium ion lost in the fluid excreted from the colon due to the laxative / purgative action.

Quantity Calculations

To understand the chemical and physiological rationales behind the formulation of the magnesium citrate component of the products, it will be necessary to determine whether magnesium oxide or citric acid is the limiting reagent, and how much of the excess reagent remains unreacted. For both taste and safety reasons, citric acid should be in a slight excess.

14. According to the formulation information, 3.5 g of magnesium oxide and 12.0 g of anhydrous citric acid are in each sachet of Picolax. Prove by calculation(s) that magnesium oxide is the limiting reagent, and that anhydrous citric acid is the excess reagent.

15. Using **Equation 3** in Question 12 calculate the theoretical yield of magnesium citrate from 3.5 g of magnesium oxide.

16. Citric acid is the excess reagent. Calculate the excess amount of citric acid (g units).

17. Using **Equation 4** in Question 13 calculate the amount of citric acid required to react with 0.50 g of potassium bicarbonate. The amount 0.50 g is given in the formulation.

18. Subtract the amount determined in Question 17 from the amount determined in Question 16 to calculate the final amount of excess citric acid.

19. Calculate the magnesium dosage in each sachet (package).

6. Heavy Magnesium Carbonate / Anhydrous Citric Acid Mixtures

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Cambridge Healthcare Products produces Citramag® purgative. This pharmaceutical product is utilized in the UK (United Kingdom) by the NHS (National Health Service). The abbreviation BP on the package = British Pharmacopeia, the UK equivalent of USP.

Formulation Information for Citramag (2025)*

From the prescribing information sheet for Citramag (12): "Citramag® is a white, lemon-lime flavoured effervescent powder in a sachet, containing magnesium carbonate, 11.57g & citric acid17.79g."

Chemical Reaction

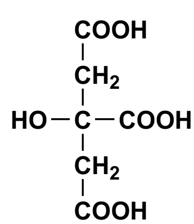
A chemical reaction occurs when the dosage of powder is dissolved in water solution. One dosage is used for a laxative effect, two doses for a purgative effect. Both the absolute amount of each substance present and the relative amounts are important in ensuring the safety and efficacy of the pharmaceutical.

*It will be assumed that the 'magnesium carbonate' in Citramag is heavy magnesium carbonate (see Section 8 below for more information about this substance) and that the citric acid is anhydrous citric acid. In 2022, the product package shown in the image and the prescribing information sheet both listed the ingredients as "heavy magnesium carbonate and anhydrous citric acid". The labelling has now been changed to "magnesium carbonate and citric acid" but the quantities are unchanged.

Chemical Reaction

Required Information

Citric Acid (a triprotic acid)
$C_6H_8O_7$ or $H_3C_6H_5O_7$ = 192.1 g/mol
Heavy Magnesium Carbonate $Mg_5(CO_3)_4(OH)_2.5\,H_2O$ = 485.6 g
Magnesium Citrate $Mg_3(C_6H_5O_7)_2$ = 451.1 g/mol



pK_a Values
3.14
4.75
6.40

As soon as the very-water-soluble citric acid begins to dissolve it reacts with the solid heavy magnesium carbonate to form soluble magnesium citrate, carbon dioxide and water:

$$\mathbf{Mg_5(CO_3)_4(OH)_2.5\,H_2O\ (s) + H_3C_6H_5O_7\ (aq) \rightarrow Mg_3(C_6H_5O_7)_2\ (aq) + CO_2\ (g) + H_2O}$$

20. Balance the chemical equation for the reaction.

Quantity Calculations

To understand the chemical and physiological rationales behind the formulation of the magnesium citrate component of the laxative/purgative, it will be necessary to determine whether heavy magnesium carbonate or anhydrous citric acid is the limiting reagent, and how much of the excess reagent remains unreacted.

21. Determine by calculation(s) whether citric acid or heavy magnesium carbonate is the limiting or excess reagent.

22. Determine the quantity of excess reagent after complete reaction.

7. Light Magnesium Oxide - MgO

The term light here refers to the low temperature of production of the magnesium oxide. Wikipedia: "Magnesium oxide is produced by the calcination of magnesium carbonate or magnesium hydroxide. .... Calcining at different temperatures produces magnesium oxide of different reactivity. High temperatures 1500 – 2000 °C diminish the available surface area and produces dead-burned (often called dead-burnt) magnesia, an unreactive form used as a refractory. Calcining temperatures 1000 – 1500 °C produce hard-burned magnesia, which has limited reactivity and calcining at lower temperature, (700–1000 °C) produces light-burned magnesia, a reactive form, also known as caustic calcined magnesia." (13)

Light magnesium oxide has numerous uses and is a major industrial chemical, $US 1.59 billion in 2023 (14, 15). Pharmaceuticals is the fastest growing use sector. Light magnesium oxide can be milled to a fine powder that is stable when dried at a temperature above 100 °C. It does not absorb moisture from the air. It can then be blended with dried anhydrous citric acid to form a stable mixture which does not react until added to liquid water. This mixture is suitable for pharmaceutical use.

8. Heavy Magnesium Carbonate - $Mg_5(CO_3)_4(OH)_2.5\,H_2O$

Magnesium carbonate is an important industrial chemical (16). The market size was about $US 0.33 billion in 2023. But magnesium carbonate or $MgCO_3$ as such is not easy to manufacture. Rather, there is a family of products referred to nominally as magnesium carbonate where each member of the family has a sectorial name. Lohman Minerals, a producer of magnesium salts, lists eight magnesium carbonate mineral formulas (17). Only one of these minerals, magnesite ($MgCO_3$), has neither water of hydration nor hydroxide ion content. The other seven all have either one or both as an integral part of the crystalline structure.

The difficulty of manufacturing anhydrous $MgCO_3$ by precipitation from an aqueous solution results from two major factors. Firstly, the very small 2+ magnesium ion has a strong mutual affinity to the oxygen of the water molecule. The ion is highly solvated in aqueous solution and most of its salts are precipitated as hydrates (e.g. $MgSO_4.7H_2O$). Secondly, concentrated carbonate ion solutions are very basic because carbonate ion is a weak base. It reacts with water, producing hydroxide ions which can co-precipitate with carbonate ions.

$$H_2O + CO_3^{2-}(aq) \rightleftharpoons OH^-(aq) + HCO_3^-(aq)$$

One member of the magnesium carbonate compound family that may be produced in a pure form with reproducible composition is the hydrated double salt called heavy magnesium carbonate (18). This salt hydrate is very insoluble in water and has a specific crystalline structure. It occurs in geological formations as the mineral dypingite. There are numerous locations around the world where this mineral occurs, including in the US and in Canada (19).

Heavy magnesium carbonate is a double salt (20):

$Mg_5(CO_3)_4(OH)_2.5\,H_2O = (MgCO_3)_4.Mg(OH)_2.5\,H_2O$ (double salt)

A double salt is a complex ionic solid with a crystalline lattice whose composition corresponds to a mixture of two simpler salts. Writing the formula as a double salt can be helpful in determining quantities for a synthesis reaction, or for writing balanced equations, but it does not provide any guide to the physical structure of the substance. The three-dimensional structure is best determined by X-ray crystallography.

Heavy magnesium carbonate is the name used by the chemical industry for this substance. It is available as a food grade and a pharmaceutical grade substance. It is probably the substance present in magnesium carbonate and magnesium citrate type supplements. It is certainly used in the formulation of Citramag.

Heavy magnesium carbonate can be milled to a fine powder that is stable to drying at a temperature above 100 ° C. It does not absorb moisture from the air. It can then be blended with dried anhydrous citric acid to form a stable mixture which does not react until dissolved in water. This mixture is suitable for pharmaceutical use.

9. Equation for the Synthesis of Heavy Magnesium Carbonate

Heavy magnesium carbonate is synthesized by reacting a soluble magnesium salt such as the sulfate with sodium carbonate in boiling water solution. The product is very insoluble. The reaction equation is the sum of five reactions occurring in the solution.

Unbalanced Equation

$$MgSO_4\,(aq) + Na_2CO_3\,(aq) + H_2O \rightarrow Mg_5(CO_3)_4(OH)_2.5\,H_2O + Na_2SO_4\,(aq) + CO_2\,(g)$$

You could balance this equation by trial and error. What follows is a systematic approach. The overall synthesis is the sum of five simple reactions.

Required Information

A. The formula of the heavy magnesium carbonate should be written as a double salt:

$$Mg_5(CO_3)_4(OH)_2.5\,H_2O = (MgCO_3)_4.Mg(OH)_2.5\,H_2O$$

B. There are five reactions occurring, each of which may be written as a separate balanced equation. The five equations will be added together to give the overall equation.

C. The source of hydroxide ion is the K_b equilibrium reaction of carbonate ion. This is a dynamic equilibrium, so more hydroxide ion is produced as the reaction to form the product heavy magnesium carbonate proceeds:

$$H_2O + CO_3^{2-}\,(aq) \rightleftharpoons HCO_3^-\,(aq) + OH^-\,(aq) \quad \textbf{(This is a } K_b \textbf{ Equilibrium Equation)}$$

D. Bicarbonate ion is unstable in hot water (21). A reaction occurs, forming carbonate ion and carbon dioxide gas:

$$2\,HCO_3^-\,(aq) \rightarrow CO_3^{2-}\,(aq) + CO_2\,(g) + H_2O$$

Steps

23. Two moles of hydroxide ion are required in the product formula. Convert the ionic equation of Point C above into a complete equation by adding sodium ions. Multiply the coefficients as needed to synthesize two moles of hydroxide ion. This is **Equation 1.**

24. The two moles of bicarbonate ion produced in Equation 1 react in hot water according to the ionic equation of Point D above. Convert the ionic equation of Point D above into a complete equation by adding sodium ions. Multiply the coefficients as needed to react the two moles of bicarbonate ion. This is **Equation 2.**

25. One mole of magnesium hydroxide is needed. Write a balanced complete equation to synthesize one mole of magnesium hydroxide. This is **Equation 3.**

26. Four moles of magnesium carbonate are needed. Write a balanced complete equation to synthesize four moles of magnesium carbonate from magnesium sulfate and sodium carbonate. This is **Equation 4.**

27. Write a balanced complete equation to synthesize a mole of double salt from 4 moles of magnesium carbonate, 1 mole of magnesium hydroxide, and 5 moles of water.
    This is **Equation 5.**

28. Sum Equations 1, 2, 3, 4, and 5. Sum the left-side and right-side reagents. Remove any duplicates occurring on both sides of the equation by subtraction.
    The resulting equation is the balanced synthesis equation.

10. Classification of Reactions

Your course outline probably contains a section devoted to classifying chemical reactions according to the type of chemical change occurring.

29. Classify the reaction(s) occurring in the following questions above. Some reactions will fall into more than one type of chemistry: 3, 6, 10. 11, 12, 13, 20, 23, 24, 25, 26, and 27.

11. Excess Citric Acid Concentrations in the Ingested Laxatives

The Picolax and Citramag formulations are intended to result in a solution of magnesium citrate containing excess citric acid. This ensures that the solution will have a pleasant, citrus fruit-like flavour. Typical citric acid concentrations for juices and beverages are known (22).

30. (a) The amount of citric acid calculated in Question 18 (Picolax) is dissolved in 150 mL of solution for ingestion. Calculate the concentration of the acid in g / L units,

    (b) Compare your answer to part (a) to the values for various fruit juices and soft drinks in Reference 22.

    (c) The amount of citric acid calculated in Question 22 (Citramag) is dissolved in 200 mL of solution for ingestion. Calculate the concentration of the acid in g / L units.

    (d) Compare your answer to Part (c) to the values for various fruit juices and soft drinks in Reference 22.

12. Potassium Ion Concentration in the Ingested Picolax Laxative

Picolax lists 0.5 g potassium hydrogen carbonate (potassium bicarbonate) as an inactive ingredient. The potassium hydrogen carbonate reacts with citric acid, providing 5 mmol or 195 mg of dissolved potassium ions as an electrolyte replacement, and carbon dioxide to carbonate the solution, making it more palatable. Loss of potassium ions is a major concern in many intestinal illnesses. By comparison to the 195 mg of potassium per dose, a 360 mL bottle of Gatorade contains 50 mg of potassium (23).

The WHO (World Health Organization) formulation for oral rehydration (24) suggests a concentration of 20 mmol/L for potassium when rehydrating, with an acceptable range 15 – 25 mmol/L .

31. (a) Verify by a calculation that the amount of potassium in the Picolax formulation is 5 mmol.

    (b) Calculate the concentration of potassium ions in the 150 mL of solution after the Picolax is dissolved in mmol/L units.

    (c) How does this value compare to the WHO recommended range

13. Sodium Saccharin Amount in the Ingested Picolax Laxative

The formulation of Picolax includes sodium saccharin. This is a synthetic sweetener (25). Suppose that the intention is to achieve a sweetness level in the ingested medication equivalent to that of apple juice, which is due to 10 g / 100 mL of glucose in the juice. The sweetness level of various substances relative to sucrose is known (26). You can calculate an approximate value for the sodium saccharin content of a sachet of Picolax.

32. (a) How much glucose would be required to achieve a level of 10 % (m / v) in the 150 mL of water containing the sachet dosage of Picolax? Answer in g units.

    (b) Convert the amount of glucose in part (a) to a mass of sucrose that is equally sweet to the taste. Answer in g units.

    (c) Convert the amount of sucrose in part (b) to a mass of sodium saccharin that is equally sweet to the taste. Answer in mg units. Assume that sodium saccharin is 500 times as sweet as sucrose.

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