Exp't 874

Isolation of Piperine from Black Pepper

Adapted by L. Grove (Penn State Univ.) from Epstein, W. W.; Netz, D. F.; Seidel, J. L. *J. Chem. Ed.* **1993**, *70*, 598-599.

Introduction:

Piperine can be isolated in good yield from ground black pepper, which is made up of 5-9% of alkaloids that also include piperidine, piperettine and piperanine and comes from the dried fruit of aschanti (Figure 1).[1] Pepper's pungency was found in 1821 to be due to piperine and piperanine.[2] Historically, pepper has been thought to cure many illnesses such as cancer, malaria, and cholera; however, today it is most commonly used as a food additive.[3]
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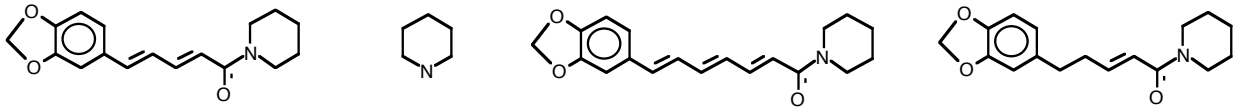
Figure 1
Alkaloids found in Black Pepper



Piperine Piperidine PIperettine Piperanine

The common procedure for the isolation of piperine involves extraction using ethanol (95%) and KOH; however, the procedure below involving refluxing with CH_2Cl_2 also gives good yield of piperine.[1] Because of the widespread uses of pepper, many synthetic approaches have also been designed for commercial production.

Cautions:

Piperine is a lachrymator; all procedures should be done in a hood.

Extraction:

Place 10.0 g of pure ground pepper and 20 mL of CH_2Cl_2 into a 100 mL 19/38 round bottom flask with a magnetic stir bar. Attach a water condenser to the top of the flask and allow water to run through it to condense the CH_2Cl_2 vapors while refluxing the solution for 20 min. After cooling the flask, use vacuum filtration with a Büchner funnel and filter paper to filter out the pepper grounds. Wash the grounds with10 mL CH_2Cl_2 and save two drops of the filtrate for TLC analysis.

Isolation and Purification:

Transfer the filtrate to a 50 mL round bottom flask and using a sand bath or rotovap, remove the CH_2Cl_2 until a dark brown oil is left. Cool the oil in an ice bath and add 6 mL of cold ether. After stirring for 5 min, remove the solvent again via sand bath heating or rotovap. Cool the oil in an ice bath and add 6 mL of cold ether again. Allow the flask to sit for 15 min in an ice bath with occasional stirring. Piperine should precipitate out; if it does not, repeat the above procedure. Using the Hirsch funnel, vacuum filter the yellow piperine crystals. Wash them with cold ether (2x4 mL) and save ~5 mg of crystals for TLC analysis.

To recrystallize, place the piperine in a test tube and dissolve it in ~5 mL of a hot 3:2 acetone:hexane solution. Let sit for 15 min at room temperature and then 30 min in an ice bath. Vacuum filter the crystal using a Hirsch funnel and wash with 4 mL of cold ether. It may be necessary to get a second crop of crystals from the mother liquor to improve yield. After dried, take a melting point of the crystals.

Cleaning up:

Dried pepper grounds can go in the trash and CH_2Cl_2, ether, and acetone:hexane can be disposed of in the proper waste containers.

Analysis:

1H and 13C NMR, MS, TLC, and IR are to be done to analyze the product. For TLC, use a 3:2 acetone:hexane solution to develop the TLC plates. Spot samples of the first filtrate, the crude piperine, purified piperine and a standard of piperine. The piperine crystals can be dissolved in acetone for spotting and visualized using a UV lamp.

Final Report:

Two other major alkaloid components of pepper are piperidine and piperettine. Explain how using ^{1}H NMR one could distinguish between the isolated piperine versus piperidine and piperettine.

Explain the trituration process and why all of the CH_2Cl_2 solvent must be removed to yield piperine crystals. (Include the explanation in your Discussion section of your final report.)

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[1] Ikan, R. *Natural Products, A Laboratory Guide*, 2nd ed.; Academic Press: New York, 1991.
[2] Oerstedt, H. *Schweigers J. Chem. Phys.* **1821**, *29*, 80.
[3] Leung, A. Y., Ed. *Encyclopedia of Common Natural Ingredients Used in Food, Drugs and Cosmetics*; John Wiley & Sons: New York, 1980.
[4] Ikan, R. *Natural Products, A Laboratory Guide*, 2nd ed.; Academic Press: New York, 1991.
[5] Oerstedt, H. *Schweigers J. Chem. Phys.* **1821**, *29*, 80.
[6] Weast, R.C., Ed. *CRC Handbook of Chemistry and Physics*, 58th ed.; CRC Press: West Palm Beach, FL, 1978.
[5] Integrated Spectral Data Base System for Organic Compounds. http://www.aist.go.jp/RIODB/SDBS/menu-e.html (accessed November 2001).