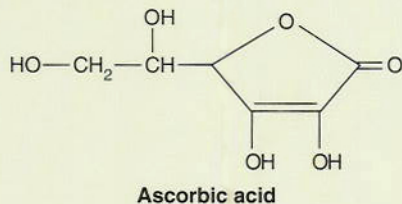



Ascorbic acid, a lactone with a molecular weight of 176.1 D, is a powerful reducing agent:



It is synthesized by all mammals except guinea pigs, apes, fruit-eating bats, and, of course, humans. These species must obtain ascorbic acid (also called *vitamin C*) in their diet. The three enzymes necessary to synthesize ascorbic acid have been isolated from microsomal fractions of liver tissue from species that can synthesize the molecule. In humans and guinea pigs, however, one of the enzymes (gulonolactone oxidase) has not been detected. (Antibodies that bind specifically to gulonolactone oxidase do not bind to human or guinea pig hepatic microsomes.) Presumably, lack of this enzyme prevents these species from synthesizing ascorbic acid.

 Scurvy (Figure 7A), the disease caused by a significant depletion of the body's stores of ascorbic acid, was common in Europe before the introduction of root crops at the end of the Middle Ages. However, as Europeans took increasingly longer voyages to search for a trade route to the Far East, outbreaks of the malady were dramatic (and often documented). For example, a ship's log written during Vasco da Gama's expedition (1498) reveals an outbreak of scurvy on the return journey across the Arabian Sea. The sailors "again suffered from their gums, their legs also swelled and other parts of the body and these swellings spread until the sufferer died, without exhibiting symptoms of any other disease." During the expedition the sailors became convinced that oranges were a curative for scurvy, whose symptoms did not appear until 10 weeks after setting sail.

When James Lind, a surgeon in the British Royal Navy, performed his famous experiment (perhaps the first controlled clinical trial) in 1746, he compared the curative effects of several treatments on 12 sailors who had scurvy. Two men were assigned to each of six daily treatments for two weeks. Briefly, the treatments



FIGURE 7A

Scurvy Grass Promoted as a Cure for the Disease

The title page of the English version of Moellenbrok's seventeenth-century book and his illustration.

were (1) 1 quart of hard cider, (2) 25 mL of elixir of vitriol three times a day, (3) 18 mL of vinegar three times a day, (4) 0.3 L of seawater, (5) two oranges and one lemon, and (6) 4 mL of a medicinal paste containing garlic and mustard seed, among other herbs. Contrary to popular opinion, Lind's work did not prove the efficacy of citrus fruits in the treatment of scurvy; these had already been an accepted treatment for several hundred years. Actually, citrus fruits were Lind's positive controls. He was apparently interested in testing the effectiveness of the official treatment of the Royal Navy: vinegar (treatment 3). The results of the trial: Those who received the oranges and lemons were fit for duty after 6 days. The other treatments varied widely in outcome but were all significantly less effective than citrus fruits. Lind subsequently reported his results to the British Admiralty, and in 1754 his work *A Treatise on Scurvey* was published. Eventually (1795), the Royal Navy approved the daily ration of 1-1/2 ounces of lime juice on all ships, giving rise to the nickname of "limeys" for British sailors.