ties can assist spectroscopists in understanding a molecule's behavior and identifying the origin of certain spectral features like symmetric and asymmetric stretches.

Not only can computational results help interpret complicated laboratory spectra, Dixon explained, but a good theoretical basis is key to understanding and predicting phenomena that cannot be measured easily in some cases or cannot be measured at all in other situations.

"There's a renaissance going on now in actinide and relativistic chemistry," Dixon said. It's being brought about by progress in theoretical and experimental techniques. "On the experimental side, it's due to advances in spectroscopic methods and synthesis. On the computational side, it comes from improvements in algorithm, software, and hardware."

Did the symposium have the effect its organizers intended? It certainly appeared to. Several times during the five-day meeting scientists could be seen rifling through their papers to see if calculated values matched measured ones and vice versa. And on the last day of the seminar, Beitz presented a uranyl fluoride Raman spectrum that he had recently annotated to show that the spectrum's main features agree well with calculated vibrational parameters reported by Dixon at the opening of the seminar.◀

Take Two Cups Of Coffee And Call Me Tomorrow

Coffee and chocolate contain antioxidants that may promote health

Sophie L. Wilkinson
C&EN Washington

From the ACS meeting

Wouldn't it be lovely if coffee and chocolate were good for you? Well, don't just roll your eyes and turn the page. Evidence presented during a symposium at the American Chemical Society's national meeting last month in Anaheim, Calif., on the chemistry and health benefits of caffeinated beverages, sponsored by the Division of Agricultural & Food Chemistry, indicates this may be so.

Coffee and chocolate products contain a range of polyphenolic antioxidants known as flavonoids, which may have health benefits such as prevention of heart disease. And there may be far more of them than are commonly accounted for, according to Joe A. Vinson, professor of chemistry at the University of Scranton, in Scranton, Pa.

Much of the work on dietary intake of flavonoids relies on Dutch research that has focused on just five flavonoids, Vinson said. But "they are not measuring all the compounds that are there," he protested. "There are 4,000 known ones, and more all the time. And I think all polyphenols are good for you."

Vinson decided to study all of the antioxidants together, excluding vitamin C. In terms of polyphenol content, he found that "coffees are lower than teas and lower than wines, but higher than just about anything else you can think of in beverages (like fruit juices)." But because Americans drink a lot of coffee, it represents their top source of antioxidants from food.

Of course, data on food samples themselves don't necessarily translate into actual health benefits. To help clarify the situation, Vinson gave coffee to hamsters for a couple of weeks and then examined the concentration of lipids circulating in their blood. Oxidation of lipids is the initial step in atherosclerosis.

Coffee consumption had no effect on the hamsters' lipid levels, but it did reduce plasma oxidation by about 30%. That indicates that "the antioxidants are preventing lipids that are circulating in the plasma from being oxidized," Vinson said. And coffee drinking tripled the hamsters' "lag time," the time it takes to oxidize the antioxidants in low-density lipoprotein (LDL)—the "bad" form of cholesterol—in a test tube. Preventing

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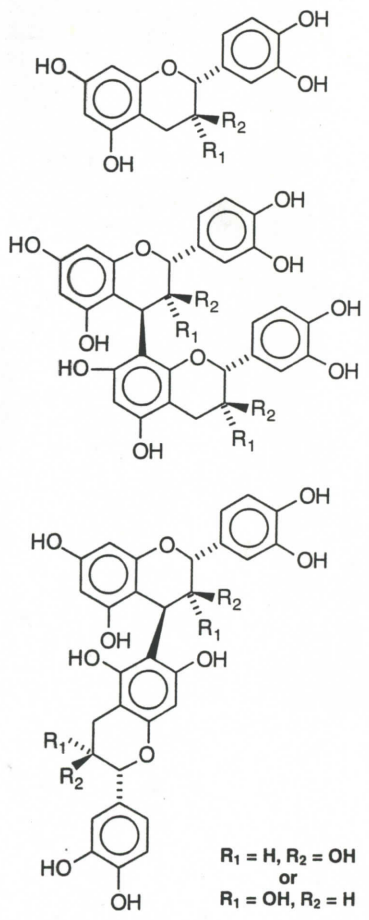
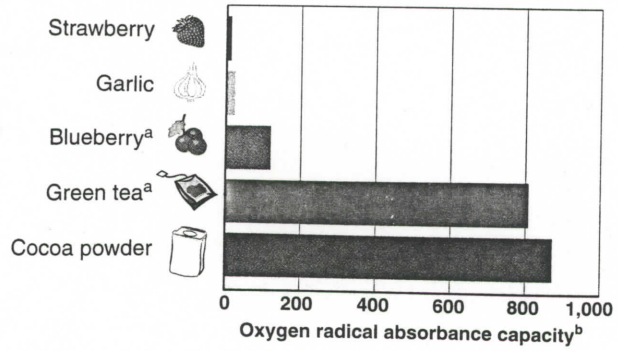
Cocoa procyanidin monomers and dimers



Cocoa powder's antioxidant capacity tops that of other good sources



a Dry weight. b Comparison in micromolar equivalents of Trolox antioxidant reference standard per gram of sample.

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LDL oxidation is believed to interfere with the onset of heart disease.

The impact on lag time represents a "very large change," Vinson said. "If you were to start taking vitamin E suddenly at 800 IUs [international units] per day, your lag time might go up 30%." He cautioned, however, that the hamsters were drinking more coffee on a weight basis than a human could. He will soon have results from long-term hamster studies.

Vinson is also studying chocolate's possible benefits. "People normally think of chocolate as bad, and it is bad in terms of calories and fat and sugar," he said. However, cocoa butter, the fat in chocolate, contains a lot of stearic acid. And that is "an unusual saturated fatty acid that doesn't raise cholesterol," said Vinson, who partakes of both chocolate and coffee "in moderation."

He found that polyphenol levels in milk chocolate, dark chocolate, and cocoa powder are extremely high on a weight basis. A 40-g milk chocolate bar contains more than 300 mg of polyphenols; dark chocolate has more than double that; and cocoa powder has about four times that. "It is loaded!" Vinson said.

The amount of polyphenols in a serving of dark chocolate is comparable to that in a cup of black tea and higher than in a glass of red wine, "the things we normally think of as great sources of antioxidants. So chocolate is extremely high in polyphenols compared to other foods. The next question is, 'Are they absorbed, do they work?'"

Harold H. Schmitz, group research manager of analytical and applied sciences at M&M/Mars in Hackettstown, N.J., has also been studying flavonoids in chocolate and cocoa. The firm, which he says is the world's leading chocolate company, is interested in procyanidin flavonoids because they influence flavor.

Schmitz and his colleagues have developed an analytical technique that for the first time can separate into individual fractions the family of procyanidins that can be found in chocolate products and other plant-based foods. Rather than using the typical reversed-phase high-performance liquid chromatography methodology—which yields "one big hump" for all the procyanidins—the Mars team used normal-phase HPLC hooked to a mass spectrometer.

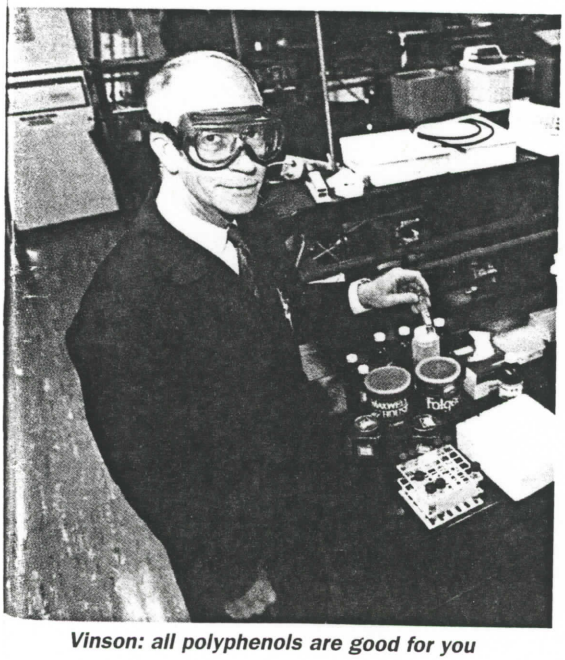
Using the new method, they determined that the procyanidins can occur as monomers or as oligomers, with two, three, or more units linked together. Because food-processing techniques affect the amount and type of these substances found in chocolate products, Schmitz cautioned that his results cannot be generalized to all such foods.

He next set out to determine whether the different procyanidin fractions show different antioxidant activity. In vitro tests showed that they had significant activity, and that an oligomer's ability to inhibit LDL oxidation rises as it increases in size. Schmitz said these results are "quite exciting, because cocoa and certain chocolates contain greater quantities of these higher oligomers than some other foods." He added that the work suggests that "not all antioxidants are created equal, not all polyphenols or flavonoids in cocoa and certain chocolates are created equal."

Schmitz believes further research is needed to assess his results. One or two in vitro experiments aren't enough to prove that chocolate can prevent heart disease, he said.

In addition to the potential cardiovascular effects of chocolate and coffee, symposium participants presented data on the effects of caffeine on the brain and on behavior. Andrew P. Smith, a professor of experimental psychology at the University of Bristol in England, combed through 10 years of literature on the impact of caffeine on cognition and mood.

In such studies, test subjects may be brought to a lab for baseline measurements and then given a cup of caffeinated coffee (instant



Vinson: all polyphenols are good for you

Chocolate alchemy

Chocolate flavor used in candy, for example, is normally made by compounding—a blending of cocoa extracts and some other chemicals, according to Chris Q. Chen, a research scientist at Universal Flavors, Indianapolis. But this natural flavoring can be expensive, so Chen has developed a new, lower cost source for chocolate flavor. Chen presented his results during a symposium on the chemistry of caffeinated beverages sponsored by the Division of Agricultural & Food Chemistry.

Chocolate preparation typically involves fermentation of raw cocoa beans, producing flavor precursors such as amino acids and sugars. The beans are then roasted to convert the precursors into hundreds of flavor compounds via the Maillard reaction.

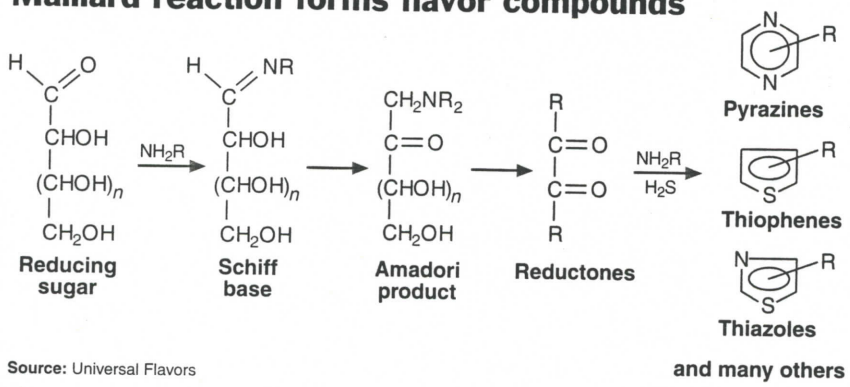
Chen's method also makes use of this reaction, in which the amino group in amino acids or peptides reacts with the carbonyl of reducing sugars. The condensation products undergo Amadori rearrangement followed by dehydration to yield furans, furan derivatives, and fission products such as reductones. These then react further, generating aroma compounds and brown pigments.

Chen wouldn't reveal specific details, but he told C&EN that he mixes amino acids including valine, leucine, isoleucine, and phenylalanine with sugars and other precursors. With the assistance of the Maillard reaction, he comes out with a product that really tastes like chocolate but costs much less than natural chocolate flavoring.

The research took three or four months. "I tried many, many reactions," Chen admitted, "and it finally came out as chocolate flavor."

The technique Chen developed can also generate peanut, coffee, or tomato flavors, depending on the precursors and processing conditions selected. The peanut and coffee flavors, for example, are derived from protein hydrolysates, which contain a number of amino acids and peptides. The most important processing variables include reaction temperature and time, followed by pH, reaction medium (oil- or water-based), and water activity. Reaction temperatures of 120 to 145 °C are ideal for chocolate flavor formation, and 160 to 180 °C are best for coffee and peanut flavors.

Maillard reaction forms flavor compounds



Source: Universal Flavors

coffee, for example, contains about 60 mg of caffeine) or decaffeinated coffee (which has less than 1 mg of caffeine). After a half hour, their performance is tested again. They are asked how alert they are feeling, and they may perform a task that requires sustained concentration. They may, for instance, have to press a button every time a particular number appears on a computer screen.

The research confirmed what millions of imbibers believe, that caffeine improves alertness and the ability to concentrate. "This is particularly beneficial when your alertness is reduced—for example, when you are sleep-deprived or when you have a minor illness like the common cold," Smith told C&EN. Because caffeine "has a very slow half-life—between three and five hours—these [beneficial] effects can go on for quite a long while."

Typical daily consumption of caffeine is around 120 to 150 mg for a 60-kg person, or 2 to 2.5 mg per kg, according to Astrid Y. Nehlig, research director at the French National Institute of Health & Medical Research (INSERM) in Strasbourg. At doses up to about 300 mg per day, caffeine induces positive effects on mood, alertness, vigilance, and feelings of well-being. But doses above 400 mg result in negative feelings, including bad mood, aggressivity, and anxiety.

These behavioral effects can be correlated with caffeine's impact on glucose metabolism in the brain, Nehlig told C&EN. At a dose of 1 mg per kg, cerebral activity increases only in a few regions of the brain. These include the caudate nucleus, which mediates locomotion, and the raphe nuclei and locus coeruleus, which are involved in the control of mood states and sleep.

As the dose rises to 2.5 mg per kg and then to 5 mg per kg, activity increases in other brain regions affiliated with locomotion, mood, and sleep, and in the amygdala—which controls anxiety levels. Nehlig noted that the caffeine in her tests is administered in a single dose rather than spread out over an entire day, so these concentrations represent quite a high dose.

Nehlig then turned to a question that has persisted for a decade: Can caffeine induce dependence? She examined caffeine's impact on the shell of the nucleus accumbens, the area in the brain involved in addiction and reward that is activated by amphetamines, cocaine, morphine, and nicotine. Her tests indicate that doses up to 5 mg per kg have no impact on activity in this area.

At 10 mg per kg, activity does increase there, "but this increase occurs in a nonspecific way," Nehlig said. "When you give caffeine at that dose to animals, you have a generalized increase in activity all over the brain, maybe 50 structures out of 60." This contrasts with drugs of abuse, which at low doses selectively activate this nucleus. Nehlig concluded that "it is very unlikely that caffeine can induce dependence by a mechanism that resembles that of the common drugs of abuse."

Nehlig compared caffeine's effects to those drugs because both act on the neurotransmitter dopamine. She plans to now check into the mechanism of dependence induced by the drugs that influence GABA (γ-aminobutyric acid) neurotransmission, including alcohol and the benzodiazepenes (such as Valium).

While some people "claim that they are totally unable to stop caffeine," Nehlig said, for most people a cup of coffee is simply a source for feelings of well-being and an upbeat mood.◀