

Nobel Prize
Research from
Japan 30Natural Product Chemistry that
Leads to MedicinesLeads to MedicinesSatoshi Omura

N ature is host to countless compounds that can be used as medicines and yet remain undiscovered by humans. Satoshi Ōmura has isolated and determined the structures of many useful natural organic compounds produced by microorganisms in soil, many of which have been put to practical use. One such compound is avermectin, a substance produced by the bacterium Actinomycetes that was isolated from the soil of a golf course in Shizuoka Prefecture. Ōmura's research in collaboration with William C. Campbell showed it has strong activity as an anthelmintic, a treatment for parasitic diseases. Subsequently, a structurally modified version of this compound, ivermectin, was



Dr. Satoshi Ōmura (1935-)

developed as an anthelmintic for livestock.
Furthermore, ivermectin has been shown to be effective against onchocerciasis, a disease which may lead to loss of sight, caused by filarial nematodes transmitted by mosquitoes in Africa and other tropical regions, and is now widely used as an anthelmintic. The 2015 Nobel Prize in Physiology or Medicine was awarded to Satoshi Ōmura, William C. Campbell, and

Chemistry Alt's Japan A Studies on Urushiol ••• Rikō Majima

U rushi lacquerware is one of Japan's well-known traditional crafts. Urushi, which has a beautiful black luster, is a natural resin obtained from the sap of the lacquer tree and consists mainly of a catechol derivative called urushiol. The structure of urushiol was determined by Rikō Majima, and the research process became the starting point for the development of organic chemistry in Japan. When Majima started his research around 1900, chemistry in Japan was still in its infancy, and there was a serious shortage of skilled chemists to guide experimental research. Majima studied organic chemistry almost entirely on his own and became acutely aware



of the gap in ability between Japan and the Western countries; at the same time he came to the conclusion that if he could conduct research on lacquer, which is native to the Orient, he would be able to develop his own original research without being outdone by researchers from other countries.

Urushiol: originally a light-yellow resin, it turned blackish after 100 years

Youyou Tu for "their discoveries concerning a novel therapy against infections caused by roundworm parasites." Youyou Tu also discovered artemisinin, which is the basis of a group of drugs used to treat malaria.



A fter studying in Germany, Majima began to determine the structure of urushiol in earnest at Tohoku Imperial University. With the latest European methods such as advanced vacuum distillation, ozonolysis, and catalytic reduction, he tried to determine the structure of urushiol. After several steps, he finally determined that urushiol exists as a mixture of the compounds shown in



Dr. Rikō Majima (1874–1962)

the figure. Majima began to determine the structures of many other natural products found only in the Orient such as indole and aconite alkaloids, in addition to urushiol, and trained many of his students as organic chemists. His students eventually established organic chemistry laboratories at universities around the country and laid the foundation for modern organic chemistry in Japan.

Figure: Structure of Urushiol



 $R = \begin{cases} -(CH_2)_{14}CH_3 \\ -(CH_2)_7CH=CH(CH_2)_5CH_3 \\ -(CH_2)_7CH=CH(CH_2)_4CH=CH_2 \\ -(CH_2)_7CH=CHCH_2CH=CHCH=CHCH_3 \\ -(CH_2)_7CH=CHCH_2CH=CHCH_2CH=CHCH_2CH=CH_2 \\ \end{cases}$

Tale related to Preparatory Problem



Green tea, a part of Japanese culture

What would you drink when you are thirsty? Water, juice, soda, or tea? Tea, particularly green tea, is very popular in Japan among other countries. Tea is classified into three major types: green tea (unfermented), black tea (fermented), and the rest such as oolong tea (semi-fermented). As introduced in preparatory problem 23, green-tea culture in Japan started in the early 1200s. The most famous form is the traditional 'tea ceremony', during which *matcha* is prepared and drunk. In addition, green tea is largely consumed as a regular beverage on a daily basis and has been associated with a variety of health benefits. Tea leaves contain several catechins such as epicatechin, epigallocatechin, epicatechin gallate, and epigallocatechin gallate, which are responsible for the characteristic taste (*shibumi*) of green tea. Japan also made significant contributions to green-tea chemistry. For instance, Michiyo Tsujimura, the first Japanese female doctor of agriculture, isolated catechin from green tea for the first time in 1929. Green tea also contains caffeine, which has a bitter taste (nigami), and theanine, which adds a savory (*umami*) flavor. While green tea is produced by suppressing the oxidation of tea leaves, black tea is produced by fermentation of the tea leaves, promoting oxidative dimerization of catechins to give theaflavins, which have a benzotropolone core structure and are characteristic pigments of black tea.

Hîmejî Castle



▼ imeji Castle (or *Himeji-jo* in Japanese) is an excellent surviving example of a modern Japanese castle. Described as a *Hirayama Jo* in Japanese, meaning a hilltop castle, it is located in the north of present-day Himeji. It is one of the original 12 castle towers (tenshu) which were built in the Edo period (1603 to 1868), and is designated as one of the 100 Great Castles in Japan. Himeji Castle was designated as a National Treasure in 1951, and a UNESCO World Heritage Site (Cultural) in 1993; so becoming Japan's first cultural World Heritage Site. The present castle tower was built in 1609 by Ikeda Terumasa, a warlord who married Tokuhime, the second daughter of Tokugawa Ieyasu, the founder of the Edo bakufu (shogunate). The castle is also known fondly as Shirasagi-jo (White Egret Castle), as its elegant figure resembles an egret with its wings outstretched. The castle is characterized by brilliant white stucco exterior walls and features a huge *tenshu* (main tower) with five layered roofs and seven stories (one underground and six above ground), which is interconnected with smaller towers (the East, the West, and the Northwest) by watari-yagura roofed passages. The tenshu was restored to its current beautiful condition after five-and-a-half years of restoration work that stretched from 2009 to 2015.







🛁 CHEER UP! Participants! 🗧

Not just IChO, but even the months leading up to it, are like a dream come true. Not only are you stimulated intellectually but you get to meet remarkable people at truly amazing places in the world. The knowledge, the drive, and encouragement you take away are unparalleled and stay with you for life.



from Maaha Ayub (Pakistan)

IChO 49th in Nakhon Pathom, Thailand Bronze Medal

Answer for Q2

4 (Cr, Ni)

Stainless steel was developed to strengthen iron's rust resistance, and a number of researchers contributed to its improvement during the 19th and 20th centuries. The metals added to iron are typically chromium and nickel, which form a passive layer on the surface, preventing rust caused by air or water. Today, stainless steel is widely used, for example, in cooking utensils, vehicles, and machine parts.

Element # 2

Japanese mineral resources

odine, with atomic number 53 and an atomic weight of 126.9, is represented by



the symbol I. It belongs to Group 17, the halogen group, together with elements such as bromine, chlorine, and fluorine. Although Japan is usually characterized as a country poor in natural resources, it is placed second in the world after Chile in the production of iodine. Eighty percent of iodine is produced from sodium iodide dissolved in ancient seawater in natural gas wells in Chiba Prefecture. Japan even exports iodine to other countries around the world.

I odine is a dark purple solid at room temperature and ¹²⁷I is its only stable isotope, with a natural abundance of almost 100%. The isotope ¹³¹I is a fission product of uranium and other radioactive elements, and it has a half-life of around 8 days transforming ¹³¹Xe with beta and gamma emissions. Therefore, stable ¹²⁷I can be used to protect people from health hazards caused by a nuclear accident. Iodine as an element has a variety of uses in our lives such as X-ray contrast agents, bactericidal disinfectants, and polarizers used in screens of LCD TVs, PCs, and smartphones.

n ince iodine is a component of thyroid hormones, a shortage of iodine

in the body may lead to the condition known as hypothyroidism. However, such shortages are rare in Japanese because the country is surrounded by sea and sufficient iodine can be obtained from a diet rich in seaweed and a variety of seafoods. By contrast, many people living in other parts of the world are exposed to the risk of iodine deficiency. Thus, potassium iodide or potassium iodate is added to the table salt to prevent it.





Chemistry! It's Cool!







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