Prostaglandins and Biologically Active Substances

1982 Nobel Prize Medicine

Sune K. Bergström, Bengt I. Samuelsson and John R. Vane were awarded the Nobel Prize in Physiology or Medicine of 1982 for their discoveries concerning prostaglandins and related biologically active substances.

Bergström, Samuelsson and Vane were able to show that prostaglandins are involved in a diverse range of biochemical functions and processes; for this reason their research opened up a new arena of medical research and pharmaceutical applications. The research has significant implications in several clinical areas, particularly in thrombosis, inflammation and allergy.

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Background

Prostaglandins were discovered in the 1930's. Ulf von Euler found that seminal fluid and seminal vesicles from most animals including man contain a substance which causes contraction of the smooth muscle of the uterus. He named this new substance prostaglandin since they were originally thought to be secreted by the prostate gland. During those decades, scientists were unaware of how these substances were produced and how they functioned. It was only after 20 years that the mysteries covering the new substance prostaglandin were uncovered by three brilliant scientists.

The Winners

Sune K. Bergström was born on the 10th of January 1916 in Stockholm, Sweden. After completion of high school, he worked at Karolinska Institute as an assistant to biochemist Erik Jorpes. Jorpes was impressed with his assistant and gave him a year-long research fellowship in University of London in 1938. Bergström returned to Karolinska Institute in 1942 and received his doctorates in medicine and biochemistry along with his M.D. two years later.

In 1945, Bergström met physiologist Ulf von Euler who was conducting research on prostaglandins. In 1947, he was appointed professor of physiological chemistry at the University of Lund where he met Samuelsson as his graduate student. Together, they conducted research on how prostaglandins are formed.Samuelsson received his doctorate in medical science in 1960 and his medical degree a year later. In 1961, he went back to Karolinska Institute to rejoin his former mentor Bergström, where he remained until 1966. He was then appointed Dean of the Medical Faculty of Karolinska Institutet, Stockholm, Sweden in July 1, 1978 until June 30, 1983.

John R. Vane was born on the 29th of March 1927 in Tardebigge, Worcester. At the age of 12, he received a chemistry set from his parents and experimentation became his consuming passion.

Vane's home became his first real laboratory and his chemical experimentation started expanding into new fields. He received his B.S. in chemistry from Birmingham in 1946 and went to Oxford University to study pharmacology. He earned his B.S. in pharmacology in 1949 and his doctorate in 1953. It was in the late 1950's when Vane developed an interest in prostaglandins.

The Discovery

During the 1950's, Bergström made an outstanding discovery and breakthrough in the field of prostaglandin research. With the use of Lyman Craig’s countercurrent extraction device, he was able to purify several prostaglandins and with the use of combination gas chromatograph and mass spectrometer, he was able to deduce the chemical structures of prostaglandins. He also discovered that prostaglandins are formed by the conversion of unsaturated fatty acids.

In the 1960's, following his successful researches, he teamed-up with Samuelsson in conducting further researches on prostaglandins. Together, they worked on how prostaglandins are formed and metabolized. They discovered that prostaglandins are formed from the progressive conversions of arachidonic acid [1], an unsaturated fatty acid. They also found that an enzyme called cyclo-oxygenase converts arachidonic acid to unstable cyclic endoperoxides from which prostaglandins, prostacyclin and thromboxanes are derived.

On the other hand, the formation of the leukotrienes from arachidonic acid is initiated by the action of 5-lipoxygenase producing leukotriene A4. Further hydrolysis of leukotriene A4 results in the formation of leukotriene B4 and C4, respectively. Because of this discovery, they were able to develop synthetic methods of producing prostaglandins and made it accessible to the scientific community.

In the early 1960's, Vane created upgrades in the procedure known as biological assay or bioassay. Bioassays are used to determine the strength of a substance by comparing its effects on an organism with a standard substance preparation. His new dynamic bioassay was used to measure more than one substance in the blood or other body fluids. By the use of this method, he learned that prostaglandins are produced by many tissues and organs and not just by the prostate.

In another study conducted in 1969, he found the methods by which aspirin alleviates pain and reduces inflammation. By the use of lung tissues of guinea pigs, Vane discovered that aspirin works by inhibiting the production of specific prostaglandins that causes inflammation. Vane also discovered the existence of prostacyclin which was found to be of great importance in dissolving blood clots.

Clinical Implications

Prostaglandins are now currently used in the treatment of ulcers, alleviating pain from menstruation and gallstones, and stimulating contractions for childbirth. Prostaglandins have also been used medically to induce abortions.

On the other hand, thromboxanes were found to be involved in the clotting of the blood. Prostacyclin acts against thromboxanes since they assist in dissolving clots. This is of great medical importance since it can be used in dissolving blood clots blocking the supply of the brain or the heart.

It is also useful in keeping blood from clotting during surgeries. Leukotrienes are found to be involved with asthma and in anaphylaxis which are characterized by contractions of the brochi. With this much knowledge in hand, medical researchers were geared towards the development of drugs and medical interventions that will exploit the use of these discovered substances.

Links
[1] http://en.wikipedia.org/wiki/Prostaglandin