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Dorothy Hodgkin and the discovery of the structure of insulin

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ABSTRACT

Despite being Nobel Prize winner, the figure of Dorothy Hodgkin is not well known beyond researchers in Biology, Chemistry and Pharmacy, and yet her discoveries, which made she worthy of being awarded the Nobel Prize, make her equally worthy of being recognized by all society. The objective of this article is to publicize her figure and place her as references for women who have achieved important milestones in the performance of their professions and whose research have been enormously useful for society. The methodology followed has been the search for information in all types of sources, both bibliographic and digital, on Dorothy Hodgkin with the proposal of showing her most notable discoveries and remarking the service she has provided to society.

KEYWORDS

Dorothy Hodgkin; Nobel Prizes women awarded; discovery of insulin; treatment of diseases.

INTRODUCTION

This article follows the same path of several others by some of the authors about women scientists who, despite having marked fundamental milestones in their academic and research careers and having discovered many fundamental active principles for curing many diseases, continue to remain largely unnoticed for society in general, since the knowledge that we have of them is scarce and is limited only to the scientific world.

Among these women, the authors dealt with several Asian and black African American women pioneers of Chemistry and Pharmacy (Núñez et al., 2022a) and (Núñez et al., 2022b), respectively, and with the American biochemist and pharmacologist Gertrude Belle Elion, awarded Nobel Prize for Medicine in 1988, who discovered drugs to treat leukemia and prevent kidney transplant rejection (Núñez et al., 2022c).

On this occasion, this article shows the biography of Dorothy Hodgkin, who, thanks to the advances she achieved in the X-ray crystallographic technique, was able to confirm the

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structure of penicillin, already proposed by the English Edward Penley Abraham (1913-1999) and the German-born British biochemist Ernst Boris Chain (1906-1979), as well as the structure of vitamin B12. Also, in 1969, after 35 years of work, she was able to decipher the structure of insulin and later determine the structures of many other biological molecules.
All this allowed her to win the Nobel Prize in Chemistry in 1964, becoming the third woman to win that Nobel Prize in Chemistry, after Marie Curie and Irene Joliot-Curie. Currently, although in the scientific field she is considered as a pioneer the studies of biomolecules by using X-ray crystallography techniques.

DOROTHY HODGKIN: HER BIOGRAPHY

On May 12, 1910, four years before the beginning of the World War, Dorothy Mary Crowfoot Hodgkin (better known as Dorithy Hodgkin) was born in Cairo (at that time Egypt was dependent on the British Empire), an event that marked her entire childhood. and his or her environment.
For the first four years of his life, Hodgkin lived in the English expatriate community in Egypt, returning to England for only a few months each year. She spent the period of the First World War in the United Kingdom under the care of relatives and friends but separated from her parents. After the war, his mother decided to stay at home in England for a year and educate her children, a period Dorothy Hodgkin later described as the happiest of her life (APA, undated). See Figure 1.

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Figure 1. A Dorothy Crowfoot Hodgkin with her mother and sisters

After completing some initial basic studies, she entered the Sir John Leman Grammar School in Beccles (a market town in the English county of Suffolk) in 1921. Only once, when she was thirteen, she did an extended visit to her parents, who had then moved to Khartoum, although both parents continued to visit England every summer. She developed a passion for chemistry from a very young age, and her mother encouraged her interest in science in general. Her public-school education left her without Latin or any other science subject, but she took private lessons to enter the Oxford University entrance exam. Only two girls were allowed to study Chemistry, being Dorothy Hodgkin (Figure 2) one of them (Ferry, 1998). At the age of 18, she began studying chemistry at Somerville College, Oxford, which was then one of the women-only colleges of the University of Oxford (APA, undated).

Figure 2. Dorothy Hodgkin in her youth

From Somerville College she graduated with first class honors in Chemistry in 1932, thus becoming the third woman to earn this distinction (Encyclopedia, undated).

After that stage, Dorothy Hodgkin decided to do her doctorate, under the supervision of Professor John Desmond Bernal at Newnham College in Cambridge, where she already realized the great possibilities that X-ray crystallography offered for the determination of

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protein structures (her advisor, John Desmond Bernal (1901-1971) was an Irish scientist who pioneered the use of X-ray crystallography in molecular biology).

Convinced of the advantages that X-ray crystallography could provide her, Dorothy Hodgkin, with the help of her advisor, began to investigate an application of this technique in the analysis of pepsin (pepsin is a digestive enzyme that is created in the stomach and that hydrolyzes proteins in the stomach, that is, it is a peptidase. It is one of the three main peptidases of the human digestive system, together with trypsin and chymotrypsin. It was the first animal enzyme to be discovered, in 1836, by the Prussian naturalist, physiologist and anatomist Friedrich Theodor Schwann (1810-1882), considered one of the founders of cell theory).

Her doctoral thesis, defended in 1937, was based on research on X-ray crystallography and the chemistry of sterols (steroids with 27 to 29 carbon atoms. Its chemical structure derives from cyclopentanoperhydrophenanthrene or sterane, a 17-carbon molecule made up of three hexagonal rings and one pentagonal).

Previously, in 1933, Dorothy Hodgkin had worked for a year at Somerville College, thanks to a research grant she had received from that institution. In 1934 she returned to Oxford University and in 1936, she became the first researcher in that university and tutor in chemistry, a post she held until 1977.

In 1937 she married the left-wing historian Thomas Hodgkin, who was a professor of adult-education in mining and industrial communities in the north of England. As his health was too poor for active military service, he continued this work throughout World War II, returning on weekends to Oxford, where his wife remained working on penicillin. They had three children, born in 1938, 1941, and 1946. Thomas Hodgkin subsequently spent extended periods of time in West Africa, where he was an enthusiastic supporter and chronicler of the emerging postcolonial states. Following an infection after the birth of her first child, Dorothy Hodgkin developed chronic rheumatoid arthritis at age 28. This left her hands swollen and distorted, yet she continued to carry out the delicate manipulations necessary to mount and photograph the tiny crystals, smaller than a grain of salt, that she used in her studies (Ferry, 1998).

In the late 1940, the future prime minister Margaret Thatcher (1925-2013), in that time Margaret Hilda Roberts was one of her students. She and Margaret Thatcher must have gotten along very well because the Prime Minister, in the 1980s and when she was already staying at her residence on Downing Street, London, placed a portrait of Dorothy Hodgkin

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there, even knowing that she supported the rival party, the Labor (Young, undated) and (BBC, 2014). See Figure 3.

Figure 3. Prime Minister Margaret Thatcher greets her former tutor, 78-year-old Professor Dorothy Crowfoot Hodgkin, before a luncheon for Nobel Laureates at Downing Street, London, 14 April 1989

In April 1953, Dorothy Hodgkin, together with other scientists who would later reach great milestones in their careers, was one of the first people to travel from Oxford to Cambridge to study the double helix model of the structure of DNA, built by later laureates with Nobel Prize the British physicist, molecular biologist, and neuroscientist Francis Harry Compton Crick (1916-2004) and the American molecular biologist, geneticist, and zoologist James Dewey Watson (born 1928), drawing on techniques developed by the New Zealand physicist Maurice Wilkins (1916-2004) and Rosalind Franklin, by the way, the this latter being unfairly ignored in that award (certainly, the work made by the British chemist and crystallographer Rosalind Elsie Franklin (1920-1958) was fundamental to the understanding of the molecular structures of DNA (deoxyribonucleic acid), RNA (ribonucleic acid), viruses, carbon, and graphite. Although her work on carbon and viruses was recognized during her lifetime, her contribution to the discovery of the structure of DNA went largely ignored. As a result, she has been described as a “wronged hero”, “forgotten hero”, “dark lady of DNA”, “feminist icon” and “the Sylvia Plath of molecular biology” (APA, undated).

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The scientists with whom Dorothy Hodgkin traveled to Cambridge were Sydney Brenner (1927-2019), a South African biologist later awarded the 2002 Nobel Prize in Physiology or Medicine), Jack Dunitz (1923-2021), a renowned British chemist and widely known chemical crystallographer, who was Professor of Chemical Crystallography at the ETH Zurich from 1957 until his official retirement in 1990, Leslie Eleazer Orgel (1927-2007), a British chemist who published more than three hundred papers in his research areas and coined the concept of "specified complexity" in his book "The Origins of Life" to describe the criteria by which living organisms are distinguished from non-living matter. His name has been popularized by the so-called two "Orgel's Laws" of evolution) and Beryl M. Oughton. According to Dr. Beryl Oughton (née Rimmer), they all traveled together in two cars once Dorothy Hodgkin announced that she was going to Cambridge to know and see the model of the structure of DNA (APA, undated)).

Later, in 1960, Dorothy Hodgkin was appointed Royal Society Wolfson Research Professor, a position she held until 1970 (Anon, 2014). This provided her with a salary, research expenses and research assistance to continue her work at Oxford University. She was a research fellow at Wolfson College, Oxford from 1977 to 1983.

Regarding her scientific achievement, Dorothy was particularly recognized for discovering different three-dimensional biomolecular structures.

In 1945, together with C. H. Carlisle, Dorothy Hodgkin published the first such structure, that of the steroid cholesteryl iodide, because she had dealt with cholesterol during her doctoral studies (Carlisle and Crowfoot, 1945). Recall that cholesteryl ester transfer protein (CETP) contributes to the transfer of cholesterol from high-density lipoproteins (HDL) to other lipoproteins, and therefore the lack of CETP affects low-density lipoprotein cholesterol concentrations. (LDL) and slows the removal of HDL cholesterol from the blood. Those affected have no symptoms but have elevated blood levels of HDL cholesterol (see Figure 4).

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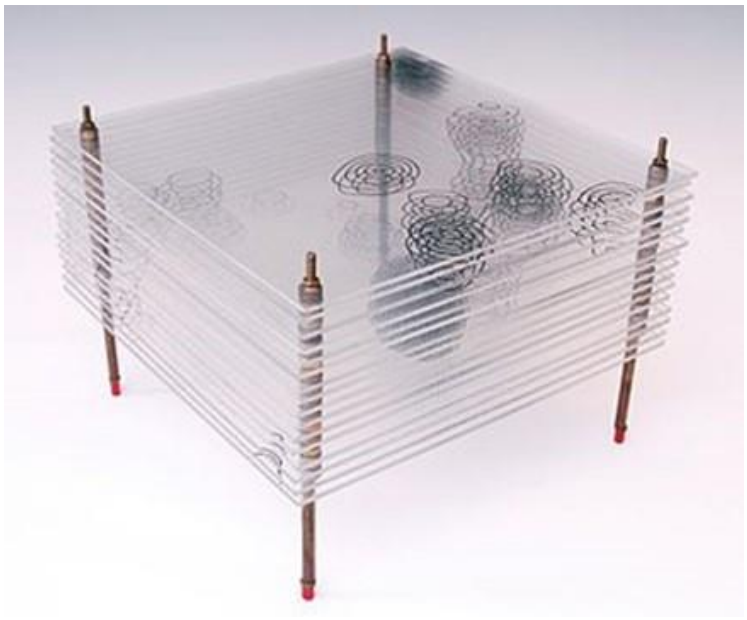

Figure 4. Model of the structure of penicillin, by Hodgkin, Oxford, c. 1945

Three years later, in 1948, Dorothy Hodgkin tried for the first time with vitamin B12 and created new crystals. This vitamin had been discovered by Merck earlier that year. Its structure at the time was almost completely unknown, and when she discovered that that vitamin contained cobalt, she realized that its structure could be determined by X-ray crystallography analysis. The fact that the molecule was large and that it was unknown enough information (which is known today) about atoms in general and not only about the one of cobalt posed a great challenge in structural analysis, not previously explored by anyone. From the vitamin crystals she deduced the presence of a ring structure since the crystals were pleochroic. This was a finding that she could confirm using X-ray crystallography. The study on vitamin B12 published by her was described by Lawrence Bragg as significantly “like breaking the sound barrier” (Brink et al., 1954). Merck scientists had previously crystallized the vitamin but had only published refractive indices of the substance. The final structure of vitamin B12, for which Dorothy Hodgkin received the Nobel Prize, was published in 1955 (Hodgkin et al., 1955). See Figure 5.

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Figure 5. Dorothy Hodgkin, Nobel Prize

With regard to the structure of insulin, this was one of Dorothy's most extraordinary research projects.

Let us remind that the origin of the discovery of insulin dates back to the second half of the 19th century. In 1869, the German Paul Langerhans, at the age of 22, described histologically a series of well-differentiated groups of cells in the pancreas, which he called “islets”, although he was unaware of their function. In 1889, the German researchers Joseph Von Mering and Oskar Minkovsky confirmed that resection of the pancreas in dogs induced a severe picture of diabetes, which led them to think of the existence of some pancreatic substance necessary for the regulation of glucose levels of the organism. In 1909, Jean de Meyer coined the poetic name “insulin” (from insula, island) to designate the substance, still unidentified, produced in the “islets of Langerhans” and which was capable of reducing blood glucose.

The first attempts to try to isolate insulin soon followed. In the first decades of the 20th century, the Romanian physician Nicolae Paulescu obtained a pancreatic extract, which he called “pancreatin”, so potent that some dogs died of hypoglycemia after its administration. Paulescu could not publish the results of his research until 1921, after the end of the Great War, although he never tried it on humans.

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The young Canadian researcher and orthopedic surgeon, Frederick Grant Banting, was the key figure in the discovery of insulin, when he became interested in diabetes when he was 14 years old and a close friend of him died of this disease. For this reason, he proposed to Professor John J.R. Macleod, Professor of Physiology at the University of Toronto, to allow him to investigate this topic during the summer of 1921 with the help of a scholar, Charles H. Best. Both young men worked by ligating the pancreatic duct of dogs to obtain trypsin-free pancreas extracts, which they called "isleton". Later, biochemist James B. Collip joined the so-called "Toronto team" and began working on obtaining the pancreatic extract, based on previous studies by Banting and Best.

Aware of these investigations, George Clowes, Eli Lilly's research director at that time, offered them the collaboration of his pharmaceutical company to obtain the elusive pancreatic extract, with the commitment of its subsequent commercialization, in case the development was viable.

After a preparation by Collip was successful when tested on a patient, a deep conflict arose between the members of the team, which was excessively aired and commented on by the scientific community itself. They even went as far as physical aggression when Banting asked Collip for the details of the preparation of his extract and he refused to provide it. Banting always argued that without his insight and input, Collip would never have come up with an extract that would serve as an effective treatment, while Macleod argued that Collip got only little help in making his discovery.

This confrontation continued and became even more evident when Macleod and Banting were awarded the Nobel Prize in Medicine in 1923. Banting denied Macleod's merits in winning the prize and shared his share of the prize with Best, while Macleod, for his part, he did the same for Collip. To this must be added the controversy over the exclusion of the Romanian scientist Paulescu from the Nobel Prize.

In addition, the story of this great discovery was trivially mythologized by a legend that presented Banting and Best as two geniuses who worked single-handedly in precarious conditions. However, these investigators probably had the best investigative resources of the day. The University of Toronto had magnificent infrastructures and an excellent documentation service. Banting, Best, Macleod and Collip were in a very appropriate time and place for their work to end in success.

Thanks to the collaboration of Eli Lilly, throughout 1922 an adequate production system for this substance was developed at the University of Toronto, marketed under the name of Íletin. The following year, the Danish August Krogh began producing insulin in Denmark, using the

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same system he had learned in Toronto. Thus he founded the company Nordisk Insulin Laboratory, now Novo Nordisk. Thus, two pharmaceutical companies, Lilly and Nordisk, very early began to dominate the world market for insulin.

Later, insulin, initially obtained from extracts of cow, pig or sheep pancreas, was purified until a recombinant human insulin could be obtained (the last paragraphs have been extracted and adapted by authors from (López and Álamo, undated)).

Moving now on the discovery by Dorothy Hodgkin of the structure of insulin, her studies on this structure began in 1934 when Robert Robinson, one of her colleagues, gave her a small sample of crystalline insulin, with which she became very interested in due to the meticulous and wide effect it had on the body. However, at this stage X-ray crystallography had not been developed enough to deal with the complexity of the insulin molecule, so she and many other researchers spent many years improving the technique. It was not until 1969 (35 years later) that the structure of insulin was finally discovered (Adams et al., 1969). See Figure 6.

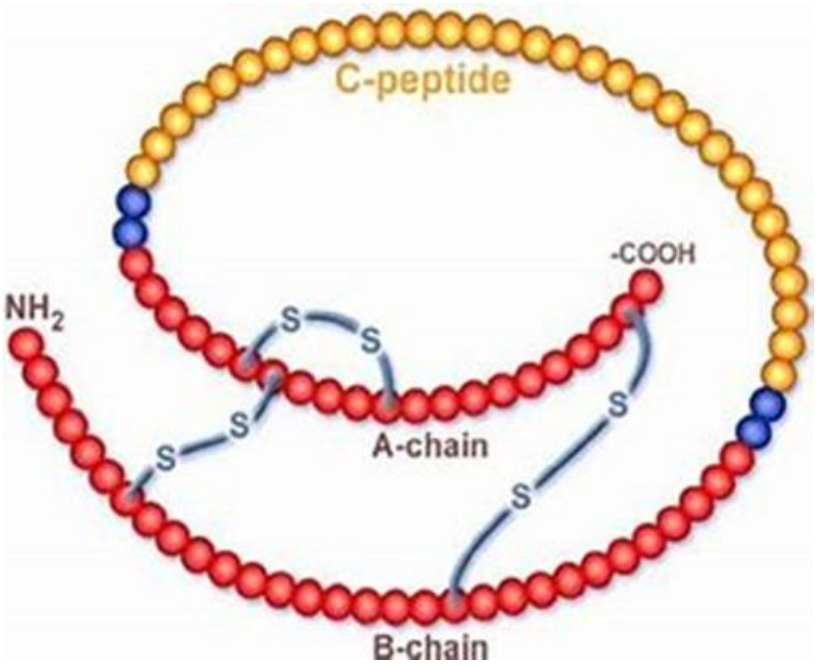

Figure 6. Structure of pro insulin showing C-peptide and the A and B chains of insulin

Between the 1950s and 1970s, Dorothy established many and long-lasting contacts with foreign scientists doing research related to hers. Thus, contacted with members of the Institute of Crystallography in Moscow, with an Indian group and another Chinese group

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working in Beijing and Shanghai on the structure of insulin. With the latter she had a very direct and fruitful collaboration.

Her first visit to China was in 1959. Over the next quarter century she traveled there seven more times. The last visit was a year before her death. Particularly successful was her visit in 1971, after the structure of insulin had been independently solved by the Chinese group, later than the Dorothy Hodgkin‘s team but at a higher resolution. During the next three years (1972-1975), while she was president of the International Union of Crystallography, she was unable to get the Chinese authorities to allow Chinese scientists to become members of the Union and attend its meetings.

Her connections with a supposed scientist in another “People's Democracy” had less happy results. At the age of 73, Dorothy Hodgkin wrote a foreword to the English edition of “Stereospecific Polymerization of Isoprene”, a work published by Robert Maxwell containing the work of Elena Ceausescu, wife of the communist dictator of Romania. She wrote of the author's “outstanding achievements” and “impressive” career. Following the overthrow of the Ceausescu during the 1989 Romanian Revolution it was revealed that Elena Ceausescu had not finished high school or attended university. Her scientific credentials were a hoax, and the publication in question was written for her by a team of scientists in order to obtain a fraudulent doctorate (Behr, 1991).

With regard to Dorothy Hodgkin's personal life, and as has been previously mentioned, her scientific mentor, Professor John Desmond Bernal, greatly influenced her life, both scientifically and politically. He was a distinguished scientist, a strong member of the Communist Party, a UK government scientific adviser during World War II, and a staunch supporter of the Soviet regime until the invasion of Hungary in 1956. Dorothy always referred to him as “Wise” (Ferry, 1998).

At the age of 24, Dorothy began to experience pain in her hands. A visit to the doctor led to a diagnosis of rheumatoid arthritis that was to progressively worsen and paralyze over time through hand and foot deformities. In her later years, Dorothy spent a great deal of time in a wheelchair, but her scientific life remained active despite her disability.

As previously stated, Dorothy married Thomas Lionel Hodgkin in 1937. The couple had three children: Luke38 (born 1938), Elizabeth39 (born 1941) and Toby40 (born 1946).

Notwithstanding her marriage, Dorothy Hodgkin published under the name “Dorothy Crowfoot” until 1949, when she was convinced by Hans Clarke's secretary to use her married name in a chapter of “The Chemistry of Penicillin”. By then she had been married for 12

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years, had given birth to three children, and had been elected a Fellow of the Royal Society. Her eldest son, Luke, remembers his mother coming home that day and announcing in a mock tragic tone, "I lost my maiden name today."

Starting that time, she has published under the name "Dorothy Crowfoot Hodgkin", and this was the name used by the Nobel Foundation on its award and in a biography in which she was listed among other Nobel Prize winners. It is also the name used by the Chemical Heritage Foundation. For simplicity, Dorothy is known as "Dorothy Hodgkin" by the Royal Society when referring to its patronage of the Dorothy Hodgkin Scholarship, as well as by Somerville College, when it opened the annual lectures in her honor.

In 1953, Dorothy Hodgkin was barred from becoming a US citizen due to her activities and that her husband was affiliated with the Communist Party and was subsequently not allowed to visit the country unless she submitted a resignation to the CIA (Rose, 1994).

In 1961, her husband became an adviser to Kwame Nkrumah, the President of Ghana. He visited the country for long periods before Nkrumah was overthrown in 1966. Dorothy was there with him when the news of his Nobel prize reached him.

Dorothy was never a communist, but she inherited from her mother, Molly, a concern for social inequalities and a determination to do everything possible to prevent armed conflict and, in particular, the threat of nuclear war. She became president of the Pugwash Conference in 1976 and served longer than anyone who preceded or succeeded her in this position. She resigned in 1988, a year after the Intermediate-Range Nuclear Forces Treaty imposed "a global ban on short- and long-range nuclear weapons systems, as well as an intrusive verification regime." She accepted the Lenin Peace Prize from the Soviet government in 1987 in recognition of her work for peace and disarmament (Howard, 1994).

In 1987, Dorothy Hodgkin decided not to attend the International Union of Crystallographic Congress in Australia for reasons of distance, although four years later, in 1993, despite his growing weakness, she surprised his close friends and family by his determination to go to Beijing for the next Congress, where it was well received by all.

Dorothy Hodgkin died of a stroke at her husband's home in the village of Ilmington, near Shipston-on-Stour, Warwickshire, on July 29, 1994 (Anon, 2014).

Both during her life and after her death, Dorothy Hodgkin has been the subject of numerous recognitions and has received many awards and distinctions, in addition to having been awarded the Nobel Prize in Chemistry in 1964, being the third woman to achieve that award

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and the only British woman scientist to have obtained it in any of the three sciences modalities of the prize, as indicated above. Apart from the Nobel Prize, among the other most outstanding prizes and distinctions the following can be mentioned.

She was also elected a Fellow of the Royal Society in 1947 (Dodson, 2002), a Foreign Honorary Member of the American Academy of Arts and Sciences in 1958 (American Academy, undated), was appointed to the Order of Merit in 1966, becoming the second woman to receive that order not being a woman in the industry life (order displayed in the Royal Society of London, Figure 7).

Figure 7. Order of Merit insignia of Dorothy Hodgkin, displayed in the Royal Society, London

She was Iota Sigma Pi National Honorary Member in 1966 (Anon, 2027), EMBO Membership in 1970 and Chancellor of the University of Bristol from 1970 to 1988 (Figure 8), foreign member of the USSR Academy of Sciences in the 1970s and she was also given an honorary Degree of Science from the University of Bath in 1978.

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Figure 8. Dorothy Hodgkin as Cancellor of the University of Bristol

In the 1980s, she had received the Lomonosov Medal of the Soviet Academy of Sciences in 1982, received the Austrian Decoration for Science and Art in 1983 (Reply a question, undated), and accepted in 1987 the Lenin Peace Prize from the government of Mikhail Gorbachev. She was the first woman to receive the prestigious Copley medal from winning the Lenin Peace Prize.

Regarding the inheritance and the legacy that her work has left to the new generations, an asteroid (5422), discovered on December 23, 1982, by L.G. Karachkina, was named "Hodgkin" in her honor (Minor Plane, undated).

She was one of five "Women of Achievement" selected for a set of British commemorative stamps issued in August 1996. The other four women were Marea Hartman (sports administrator), Margot Fonteyn (ballerina/choreographer), Elisabeth Frink (sculptor) & Daphne du Maurier (writer). All except Hodgkin were Dames Commander of the Order of the British Empire (DBEs).

In 2010, during the 350th anniversary of the founding of the Royal Society, she was the only woman in a set of stamps celebrating ten of the Society's most illustrious members, taking her

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place alongside Isaac Newton, Edward Jenner, Joseph Lister, Benjamin Franklin, Charles Babbage, Robert Boyle, Ernest Rutherford, Nicholas Shackleton and Alfred Russel Wallace (new Scientist, undated).

"For outstanding scientists at an early stage of their research career who require a flexible working pattern due to personal circumstances, such as parenting or caring responsibilities or health-related reasons", the Royal Society of London awards the Dorothy Hodgkin Fellowship (named in her honor) (Anon, 2017).

The Council offices in the London Borough of Hackney and buildings at University of York, Bristol University and Keele University are named after her, as is the science block at Sir John Leman High School, her former school.

In 2012, Hodgkin was featured in the BBC Radio 4 series The New Elizabethans to mark the diamond Jubilee of Queen Elizabeth II. In this series a panel of seven academics, journalists and historians named her among the group of people in the UK "whose actions during the reign of Elizabeth II have had a significant impact on lives in these islands and given the age its character" (BBC, undated).

Moreover, since 1999, the Oxford International Women's Festival has presented the annual Dorothy Hodgkin Memorial Lecture, usually in March, in honor of Hodgkin's work (Festival, undated).

It also deserves to be highlighted that she has been portrayed on several occasions to commemorate important events. Thus, the National Portrait Gallery, London listed 17 portraits of Dorothy Hodgkin (Collection, undated) including an oil painting of her at her desk by Maggi Hambling and a photograph portrait by David Montgomery (Digital Collections, undated).

Graham Sutherland made preliminary sketches for a portrait of Dorothy Crowfoot Hodgkin in 1978. One sketch is in the collection of the Science History Institute and another at the Royal Society in London, although the portrait was never finished (the Royal Society a and b, undated).
Finally, a portrait of Dorothy Hodgkin by Bryan Organ was commissioned by private subscription to form part of the collection of the Royal Society. Accepted by the president of the society on 25 March 1982, it was the first portrait of a woman Fellow to be included in the Society's collection (Nobel Prize Orgainization, undated).

CONCLUSIONS

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The author believes that the life of Dorothy Hodgkin deserves to be known by all of society, not only because of the important discoveries she made throughout her scientific career, highlighted in the previous section, but also because of her social behavior and her efforts for fighting against any type of war in the world, since she never forgot the hardships and sufferings that the family went through in her childhood during the period of the First World War.

The importance of her scientific discoveries has already been sufficiently described in previous paragraphs. In this regard, she described herself as "captured for life by chemistry and by crystals" (Nobel Prize Orgainization, undated). These discoveries not only allowed researchers to better understand and manufacture life-saving substances, but also helped propel crystallography as an indispensable scientific tool.

Furthermore, she always believed in international scientific cooperation and so, during the Cold War, she insisted on including Chinese and Soviet scientists in American scientific organizations, such as the International Union of Crystallography which she helped found. Likewise, she was always a staunch defender of world peace, thanks to the ideas her mother instilled in her during her childhood. In this regard, she wrote in 1981, at age 71, the following (Nobel Prize Orgainization, undated): "How to abolish arms and achieve a peaceful world is necessarily our first objective"
For all these reasons, it is clear that Dorothy Hopkin (Figure 9) can be considered a reference to the rest of the women, as a model and example to follow for all of them. As she herself wrote: "I believe in perfecting the world and trying to do everything to improve things, but not because I know what's to come of it" (Nobel Prize Orgainization, undated).

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Figure 9. Dorothy Crowfoot Hodgkin with models and crystallography images of the molecules she studied

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