



Yellapragada Subba Rao: The Unsung Hero of Science

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Abstract

This essay explores the life and work of Dr. Yellapragada Subba Rao, an Indian scientist whose contributions to medical science have profoundly impacted the world. From his early days in India to his time at Harvard University, Subba Rao's innovative research led to the development of several important drugs, including the first chemotherapy agent for leukemia and the discovery of diethylcarbamazine for filariasis treatment. Despite his many achievements, Subba Rao never received the recognition he deserved during his lifetime. However, his legacy lives on through the countless lives he has saved and the ongoing research inspired by his work. This essay sheds light on the critical contributions of Subba Rao to medical science and the remarkable impact his work has had on society.

Keywords Yellapragada Subba Rao · Indian scientist · Legacy · Medical science · Recognition

1 Introduction

Throughout history, the world has been graced with brilliant scientists whose discoveries have shaped our understanding of the universe and revolutionized our lives. From Wilhelm Roentgen's pioneering work with X-rays to Marie Curie's groundbreaking research on radium, many scientists have been recognized for a single discovery that has left an indelible mark on society. Some have been fortunate enough to be recognized for multiple discoveries, such as Albert Einstein's contributions to photoelectricity and relativity. Other Nobel Laureates whose contributions to science have left an indelible mark on society include Richard Feynman for his work in quantum mechanics, James Watson and Francis Crick for their discovery of the structure of DNA, and Kary Mullis for his invention of the polymerase chain reaction (PCR) technique that revolutionized DNA analysis. Still others, like Jonas Salk and Michael Heidelberger, have made significant contributions to their fields but have yet to receive the recognition they deserve. Among these great minds are the scientists of India, who have produced a wealth of scientific talent throughout history, from the

mathematical genius of Aryabhata to the Nobel Laureate CV Raman. Their contributions to science and technology continue to inspire and shape our world today. In the world of science, it is a rare feat for an individual to make groundbreaking contributions across multiple fields, let alone without receiving the recognition they deserve. Such was the case with Dr. Yellapragada Subba Rao, an Indian biochemist and pharmacologist who left an enduring impact on medicine. Despite being overlooked by many, Subba Rao's pioneering work has been hailed as revolutionary, particularly for discovering folic acid and its application in developing chemotherapy for cancer. Despite facing financial constraints and discrimination, his unwavering dedication to research is a testament to his remarkable character and enduring legacy. Indeed, Subba Rao's contributions to science continue to influence modern medicine, making him a notable figure in science and medicine.

2 Early life and education

Yellapragada Subba Rao was born into a family of humble means on January 12, 1895, in the small town of Bhimavaram in the Indian state of Andhra Pradesh. Despite facing financial hardship, his mother was determined to ensure that her children succeeded in life and was willing to make great sacrifices to make that happen. When Subba Rao was just 14 years old, he attempted to break free from the constraints of his family's poverty by running away from home with

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Fig. 1 Dr. Yellapragada Subba Rao: Scientist, innovator, and life-saver. Image source: Bharti and Marfatia (2017). https://doi.org/10.4103/ijdv1.IJDVL_1018_16

a cousin, hoping to make a fortune by selling bananas to pilgrims in Varanasi. This was not the first time he had tried to strike out on his own, as he had also attempted to become a monk at the age of 18. However, both times, his parents convinced him to continue his studies. After the death of his father, Subba Rao's mother sold her jewellery to ensure that he could continue his education. Despite facing numerous challenges, including the trauma of his father's death, Subba Rao persevered and eventually passed his matriculation examination after his mother's selfless sacrifice enabled him to return to Madras for a third attempt. From a young age, Yellapragada Subba Rao was driven by a desire to make a meaningful impact on the world. As a student at Madras Presidency College, he contemplated various paths, including political activism, philanthropy, and spiritual pursuits. Ultimately, he was drawn to the Ramakrishna Mission, where he studied comparative religion and was encouraged to pursue a medical career. However, Subba Rao's devotion to yoga and his spiritual beliefs initially caused him to view medical school as a temporary occupation. As he delved deeper into his studies, he began to see the importance of the doctor-patient relationship and the potential for medicine to improve the lives of those around him (Fig. 1).

Despite obstacles such as his mother's disapproval of his decision, Subba Rao dedicated himself to becoming an

accomplished physician and scientist, driven by a sense of duty to humanity (Gupta, 1976). He was on the brink of death from a severe case of diarrhea resembling sprue but was miraculously saved by Dr. Achanta Lakshmi Pathi, an Ayurvedic practitioner, after the top allopaths in Madras had failed to cure him. His desire to participate in the Non-cooperation Movement was hampered by the fear of being labeled a failure and being sent to a lunatic asylum. However, his nationalist views and traditional Indian clothing offended the European professors, especially his surgery professor, M. C. Bradfield, and he could only attain a lesser LMS degree despite his diligent efforts. While at college, he met John Fox Kendrick, a Rockefeller investigator from the United States who introduced him to research opportunities at Harvard School of Tropical Medicine, where he was admitted to study under the renowned Dr. Richard Strong. During this time, tragedy struck when his elder brother, Purushottam, who was funding his scholarship, died from tropical sprue, followed a week later by his younger brother, Krishnamurthy, who also fell ill with a similar ailment (Narasimhan, 2003). These devastating events solidified his resolve to fight against diseases, but unfortunately, with Purushottam's passing, the scholarship he relied on for his Harvard studies was no longer available (Gupta, 1976).

After being rejected from the Madras Provincial Medical Service, he found employment with Dr. Lakshmi Pathi at the Madras Ayurvedic College as a physiology lecturer, where he was able to incorporate his knowledge of Western medicine into Ayurvedic practices (Bhargava, 2001). Although he saw this as only a stepping stone towards his ultimate goal of healing the sick through foreign education at a prestigious university, he was impressed with the principles of diagnosis and treatment in Ayurveda. He believed that the *tridoṣa* theory could be tested using modern endocrinology, which suggests that health and sickness result from the harmonious or discordant interplay of protoplasm, metabolic processes, and neuro-muscular activity. His desire to integrate herbal drugs into modern medicine was initially met with discouragement from experts like Dr. Strong and Dr. Charles Sajous, but after Subba Rao renounced his original plan, Dr. Strong agreed to admit him into the post-graduate program in tropical medicine at his Boston school (Gupta, 1976).

3 Life in the United States: Fiske-Subba Rao's Phosphorus estimation method

Subba Rao arrived in Boston on a crisp fall day in 1923. He carried only \$100, which fell \$50 short of the tuition fee required for him to enroll at the School of Tropical Medicine. Luckily, Dr. Strong, struck by Subba Rao's



fervor and unshakable belief in his destiny, helped him navigate the admissions process. Despite being a qualified physician, Subba Rao found himself taking the job of washing bedpans and urinals at Peter Bent Brigham Hospital to make ends meet during his time at school. One of Subba Rao's early projects, which involved cultivating *Entamoeba coli* in the laboratory, wasn't particularly successful. However, it taught him valuable research procedures, and by June 1924, he earned his Harvard diploma in tropical medicine (Gupta, 1976). Unfortunately, he was restricted by the terms of his scholarship and couldn't use it to pursue his interests in law or general medicine. So, he switched to the Department of Biochemistry at Harvard Medical School. Biochemistry was not concerned with diseases at the time, except as they related to normal metabolic processes. Subba Rao's passion for conquering diseases led him to this field. Working under the guidance of Cyrus Hartwell Fiske, Associate Professor of Biochemistry, Subba Rao developed a rapid colorimetric method for estimating inorganic and organic phosphorus, organic phosphates, and lipid phosphorus in blood and urine within a few short months (Fiske & Subbarao, 1925). This method, known as the Fiske-Subba Rao Method, was adopted by the American Society of Biological Chemists on December 29, 1924. It has been described in biochemistry textbooks since 1925 and has become a staple in clinical and biological material analysis worldwide. After he researched the Fiske-Subba Rao method of phosphorus estimation, Subba Rao's efforts were rewarded with the awarding of a Ph.D. degree at Harvard's Commencement Program in June 1929 (Gupta, 1976). This achievement marked him as the first Indian to earn a Ph.D. from Harvard University, showcasing the exceptional caliber of his academic achievements (Gupta & Milford, 1987). Subba Rao's contribution to science may seem modest, but it was during his time as a biochemistry apprentice that he made a groundbreaking discovery.

4 Muscular energy: phosphocreatine and ATP discovery

Using a new colorimetric method, Subba Rao found periodicity in the rise and fall of urine and blood phosphate levels. This led him to conduct experiments on cats, studying the effects of fasts and special diets on their phosphate levels. He discovered that their phosphate level dropped to a tenth of the average within an hour of their last meal when they were on a sugar-only diet. Subba Rao believed he had discovered how insulin rapidly reduces blood sugar levels. Encouraged by his departmental chief Otto Folin and mentor Cyrus Hartwell Fiske, he worked tirelessly for 18 months to prove his theory on the unknown phase of sugar metabolism

that had previously baffled many, including Nobel Prize winner Frederick Banting. Although his work did not solve the insulin puzzle, it did help unravel one of the mysteries of life through a related series of experiments (Gupta, 1976). Fiske and Subba Rao embarked on a series of experiments to verify the widely held belief that the breakdown of glycogen to lactic acid releases the energy required for muscular contraction. Their hypothesis hinged on the assumption that the speculated hexose phosphate, formed by the combination of blood sugar and phosphorus, was responsible for breaking down glycogen to lactic acid (Gupta & Milford, 1987). However, the experiments they conducted in Boston failed to demonstrate that administering insulin to animals made diabetic by removing the pancreas increased hexosephosphate levels in muscle and liver (Narasimhan, 2003). The analytical methods available then could not detect sugar phosphates quickly converted by body enzymes to lactic acid.

Nonetheless, the extensive study of the organic phosphorous compounds in muscle conducted by Fiske and Subba Rao showed that the hypothesis of Otto Meyerhof and Archibald Hill was not the key to muscular contraction, despite their mistaken conclusion from the experiments with diabetic animals (Gupta, 1976). The studies conducted by Fiske and Subba Rao revealed two new compounds in muscle tissue: phosphocreatine (Fiske & Subbarow, 1928) and adenosine triphosphate (ATP) (Fiske & Subbarow, 1929). These compounds play a direct role in muscular contraction. When a nerve impulse triggers muscular contraction, actomyosin decomposes ATP, an enzymatic protein in the muscle. This process causes the actomyosin molecules to shorten, resulting in the contraction of the muscle as a whole. However, phosphocreatine then resynthesizes ATP, allowing the actomyosin molecules to return to their normal length and the muscle to its original size. This high energy transfer from ATP's terminal molecule to the muscle is responsible for the movement of limbs, lifting weights, and pumping of blood through arteries and veins. These discoveries discredited the Nobel Committee's hasty award to Meyerhof and Hill for connecting the lactic acid cycle to muscular contraction in 1922.¹ Unfortunately, priority controversies arose due to Fiske's conservative publication policy and the quick response of Meyerhof and Hill's teams to Fiske and Subba Rao's work, which clouded the rightful recognition due to Fiske.

Subba Rao's career at Harvard was also ruined due to his failed attempt to succeed Folin as Departmental Chief. Throughout their research, Fiske guided Subba Rao as needed but allowed his assistant to take the lead in setting

¹ The Nobel Prize in Physiology or Medicine 1922, NobelPrize.org, 2023.



up experiments and analyzing results. Though the discovery of phosphocreatine and ATP was primarily credited to Subba Rao, Fiske's role in the work was still significant. When Fiske's position at Harvard was in jeopardy in 1935, Subba Rao wrote a letter to the university's President stating that Fiske was the mastermind behind the research, despite Fiske's acknowledgment of Subba Rao's contribution (Gupta, 1976). This letter did not prevent an outsider from being appointed as head of the Biochemistry Department, but it did impede Subba Rao's progress at Harvard. Despite this setback, Subba Rao remained grateful to Folin, who had brought him into the department and helped him secure funding and opportunities to further his research, including a Rockefeller fellowship.

Subba Rao's dedication to his research was so consuming that it took him six years to fulfill the requirements for a Harvard Ph.D. due to his focus on auxiliary subjects (Narasimhan, 2003). Unfortunately, his extended stay in America caused his wife and her family to feel betrayed, especially after the loss of their child (Gupta, 1976). Despite this strain on his personal life, Subba Rao would have been willing to return to India if he could continue his work in biochemistry. However, his expected appointment at the All India Institute of Hygiene and Public Health in Calcutta, which Rockefeller funded, did not materialize (Gupta, 1976). Even with Folin's intimate knowledge of Subba Rao's contributions, the best he could offer was a Teaching Fellowship, typically reserved for American graduate students pursuing their doctorate at Harvard (Gupta, 1976). Unlike American Ph.D. candidates appointed as Instructors or Associates, Harvard had no opportunity to offer Subba Rao a faculty position.

5 Liver's anti-anaemia substance and diethylcarbamazine breakthrough

While Subba Rao was facing disappointment in his career and personal life, he found solace in his research on pernicious anaemia. He had been working on this project for eight years after Boston physicians Dr. George H. Minton and Dr. William P. Murphy discovered that liver meals had curative properties for the disease. Despite limited resources due to his other research obligations, Subba Rao persisted and isolated the curative principle in the liver through a charcoal adsorption and ethanol elution procedure in 1935 (Gupta, 1976). His liver concentrate proved to be as effective as the original liver meals used by George Minot and William Murphy to treat their patients, with just 15 mg of the concentrate sufficient for injection. Following Fiske's departure from research and the arrival of Dr. A. Baird Hastings as the new Departmental Chief, Subba Rao found himself with

more time to focus on liver work but little support from Harvard (Gupta, 1976). Despite not having a faculty appointment, he was assigned some assistants, who were medical undergraduates working part-time for fellowships to pay their tuition. However, he had to rely on outside analytical laboratories and a drug company for material and workforce assistance.

Progress was slow in isolating the anti-pernicious anaemia factor and two other vitamins—nicotinic acid and pantothenic acid—found in the liver (Subbarow et al., 1938, 1945). Although Conrad Elvehjem and Roger Williams were credited with discovering other vitamins, Tom Spies, Subba Rao's medical collaborator, was surprised that proper facilities were not provided for him and wrote to Hastings requesting that Subba Rao be given the necessary resources or released to the University of Cincinnati. Despite his promotion to the junior faculty post of "Associate" in September 1938, Subba Rao found the collaborative assistance promised him unsatisfactory and arrived too late. As a result, he was open to drug company executives who were eager to utilize his expertise. Lederle Laboratories, who had profited from Subba Rao's liver extracts, convinced him to move to Pearl River, New York, in May 1940 to become the Associate Director of Research and open up the field of vitamins and antibiotics for the company (Gupta, 1976). Subba Rao brought in a team of young, highly qualified university graduates who were open to the discoveries in the field. Within four years, they developed their synthetic vitamin processes, breaking through the patent monopolies of the established leaders in the US drug industry. By mid-1941, when H.W. Florey and N.G. Heatley travelled to the US to collaborate on large-scale penicillin production for World War casualties, Subba Rao had already created a purer and more potent product than the one they had produced at Oxford.

However, Lederle's management's overconfidence and distrust of "socialism" resulted in Subba Rao's penicillin group being isolated from the trans-Atlantic "pool" that was successful in producing penicillin on a large scale (Gupta, 1976). Despite this setback, Subba Rao's team used the experience to make a breakthrough in antibiotic therapy, and his group was the last to join the production of penicillin. Following the United States' entry into the Pacific wars after the devastating attack on Pearl Harbour in 1941, Subba Rao undertook a new research project aimed at safeguarding soldiers in the tropical regions of Southeast Asia. He focused on developing a non-metallic drug that could be taken orally and combat parasitic infections. This endeavour eventually led to the discovery of diethylcarbamazine. This piperazine compound has since been recognized by the World Health Organization as a critical weapon in the fight against filariasis, both as a treatment and a preventative measure (Bharti & Marfatia, 2017; Hewitt et al., 1947).



6 The discovery of Aureomycin

In the spring of 1944, Subba Rao initiated a program to screen for Actinomycetes, which appear bacteria-like but grow like fungi. This program led to the discovery of Aureomycin, the first tetracycline “broad spectrum antibiotics” that effectively combat bacterial and viral fevers (Gupta & Milford, 1987). The golden yellow mold from which Aureomycin was derived was discovered by Benjamin Duggar, an expert in fungal diseases of plants who brought a fresh approach to the world of Actinomycetes. Joseph Niedercorn, a new organic chemist in fermentation technology, successfully grew the mold in large tanks of nutritive broth and yielded the antibiotic in significant amounts (Gupta, 1976). Charles Pidack, an experienced purification expert in penicillin and streptomycin, needed the assistance of George Krupka, a technician with no scientific education, to recover the antibiotic from the fermentation mash and obtain pure Aureomycin (Gupta et al., 2013). This was a significant achievement, as it was an antibiotic developed by amateurs, inspired by Subba Rao’s pursuit of a cure for all human fevers. Despite resistance from the company’s financial and medical directors during the post-war recession, Subba Rao successfully developed Aureomycin in November 1947 (Gupta et al., 2013). However, its initial tests compared to penicillin and streptomycin did not yield positive results in test tubes and animal studies. Subba Rao decided to test its effectiveness against viral infections in humans and approached Dr. Louis Tomkins Wright, a renowned black surgeon, who was willing to test it at his Harlem Hospital in New York City against lymphogranuloma venereum (viral VD) (Gupta, 1976).

The results were astonishingly positive, and Aureomycin proved to be the first effective treatment for viral infections. This breakthrough convinced Perrin Long, the American pioneer in sulpha and penicillin therapy, that bacterial infections might respond to Aureomycin differently in humans than in guinea pigs. The first trial of Aureomycin by Long’s associates in a girl suffering from a urinary tract infection was successful, and it began its long crusade against infections that were immune to sulpha drugs, penicillin, and streptomycin (Gupta, 1976). Unlike other antibiotics, tetracyclines can be taken orally and have singular virtuosity in checking a wide range of fevers caused by bacteria, rickettsiae, and viruses, making elaborate laboratory tests unnecessary for diagnosis of many common infections and cutting down the need for hospitalization of fever victims (Gupta et al., 2013).

7 Tropical sprue factor combat: folic acid

During his time with Lederle, Subba Rao pursued the elusive “sprue factor” that would provide a cure for tropical sprue, the disease that had taken his brother’s life. His search began

with examining clinical reports, which indicated that tropical sprue was distinct from pernicious anaemia. After extracting potent fractions for pernicious anaemia, Subba Rao isolated the “sprue factor” from the residual liver. After two years of hazardous experimentation and patient responses, the “sprue factor” was eventually discovered in a chick growth factor isolated from liver and microbial fermentation broth (Narasimhan, 2003). Subba Rao’s organic chemists were able to synthesize folic acid, a new vitamin, using this information. The discovery of folic acid led to the cure of a sprue patient by Dr. William J. Darby, and it was also briefly used to treat pernicious anaemia patients. However, Subba Rao was not convinced that folic acid was the true adenosine phosphosulfate fraction (APAF), as patients who regained their normal blood picture with folic acid suffered a relapse of their neurologic abnormalities.

In the closing months of 1947, Subba Rao retrieved a liver fraction that had been on the shelf since 1941 due to his “color prejudice.” Although the fraction had a beautiful pink color, Subba Rao attributed it to the toxic chromium compound, Reinecke salt, and did not use it in patients (Gupta & Milford, 1987). His isolation chemist attempted to remove the pink color but could not do so without draining off the liver fraction’s APAF activity (Gupta, 1976). After much hesitation, Subba Rao finally allowed the pink fraction to be tested clinically. To his amazement, just 33 drops of it caused remission in a pernicious anaemia patient treated by Tom Spies in Havana, Cuba. Following this success, a second patient in Alabama was also cured. However, Subba Rao’s quest for APAF ended when Merck, a rival research laboratory, announced that they had isolated a crystalline pink Vitamin B12 specific to pernicious anaemia (Narasimhan, 2003).

Merck had obtained the vitamin in a concentrated form from the liver, but their final product was derived from grisein broths and not the liver, where the B12 occurs in bound forms and gets destroyed during fractionation (Gupta, 1976). This finding led to the conclusion that the original 1926 Minot-Murphy miracle was achieved through the 0.6 mg of folic acid in raw beef meals rather than the unasimulated 0.06 mg of B12 found in the unappetizing meal, which patients could not assimilate due to their atrophied stomach walls (Gupta & Milford, 1987). It was also discovered that the vitamin had to be administered directly into the bloodstream of pernicious anemia patients (Gupta, 1976).

8 Teropterin: chemotherapeutic drug discovery

In 1943, Dr. Richard Lewisohn of Mount Sinai Hospital in New York requested a supply of folic acid from Subba Rao to research chemicals that could reverse malignant tumors



in mice. His group had previously found success with spleen and yeast extracts, both rich sources of Vitamin B Complex. Subba Rao's folic acid was many times more effective than its previous inhibitor, inositol, in inhibiting cancer cell growth. Further experiments, supported by Subba Rao's funds and supplies, showed that folic acid could cause the complete disappearance of spontaneous breast cancer in 45 percent of treated mice (Narasimhan, 2003). Despite pressure from physicians and company executives, Subba Rao resisted clinical vitamin testing in cancer patients. When it was discovered that folic acid isolated from the liver was chemically and microbiologically different from folic acid secured from fermentation broths, both were tested by Lewisohn (Gupta, 1976). The Mount Sinai Report found that liver folic acid promoted breast cancer growth in mice, while fermentation folic acid caused complete regression of tumors in 40 percent of cases. This led to high hopes for a cancer cure, with research groups requesting Teropterin, the name given to fermentation folic acid with three glutamic acid groups instead of one in liver folic acid (Narasimhan, 2003).

In early 1947, Subba Rao synthesized Teropterin and made it available to Dr. Lewisohn for research on its potential for treating human cancer patients. To investigate Teropterin's effects further, Subba Rao established a cooperative program among several hospitals in Boston and a clinical study led by Dr. Wright at Harlem Hospital. Dr. Lewisohn presented the most notable report at the International Cancer Research Congress in Missouri, describing how Teropterin had significantly extended life and reduced the pain of Babe Ruth, the famous American baseball player who had nasal and neck cancer. However, Teropterin was not a cancer cure, as its effects on breast tumors in mice and temporary shrinking of tumors in patients were never fully understood (Gupta & Milford, 1987). All groups reported that Teropterin had a palliative effect on the central nervous system due to the release of glutamic acid when it broke down into folic acid (Gupta, 1976). Teropterin increased interest in folic acid derivatives for cancer chemotherapy despite its limitations. It led to a breakthrough that has stood the test of time with over 25 years of clinical testing worldwide.

9 The magnum opus and death

Amidst pursuing medical advancements, a Boston newspaper columnist acknowledged Subba Rao's work. However, the limelight predominantly centered around Sidney Farber, overshadowing the achievements of Subba Rao (Farber et al., 1948). Subba Rao, however, was content with this arrangement, as his friend had managed to arrange clinical trials smoothly, something that Subba Rao had struggled with regarding folic acid and Aureomycin. He had declined

honors for the Harvard work on the phosphates, stating that he had only played a minor role in the project. Despite this, he was eventually drafted as one of the 16 co-authors of the published paper about folic acid, for which he had personally organized the isolation, synthesis, and clinical trials (Gupta, 1976). Subsequently, he felt that the youngest member of the folic team, Coy W. Waller, had not received enough recognition for his innovative shot-gun synthesis process, which had been essential to obtaining an ample supply of folic acid. As a result, Subba Rao pushed Waller to the forefront, allowing him to present Teropterin to the medical community.

Subba Rao himself was seen discussing his proposal for a new cancer research laboratory with Miss Doris McKenzie, who was a medical technician and had climbed the ranks from assistant to head of the bacteriology group and from her screening program at Pearl River; she later developed cancer drugs TEM and TEPA. This conversation occurred while Dugger presented Aureomycin as the "discoverer" at a conference for the New York Academy of Sciences on July 21, 1948 (McKenzie & Stadler, 1948). On August 8, 1948, Subba Rao spent his last day working diligently at the Pearl River laboratory, where he had made many significant contributions to medical science. That evening, after reading the local newspaper, he placed it and his reading glasses on the bedside chair and peacefully passed away in his sleep (Gupta, 1976). Although he died unknown to many, his legacy lives on through the countless individuals who have benefited from the drugs he envisioned and created. American writer Doron Antrim once said in the April 1950 issue of *Argosy*, "You've probably never heard of Dr. Yellapragada Subbarao. Yet because he lived, you may be alive and are well today. Because he lived, you may live longer." Even now, there are still many who have yet to learn about his important work and the impact it has had on the world. After his passing, Subba Rao's ashes were kept in the home of Merton Lockhart, a close associate who held deep respect and admiration for him.

10 Conclusion

Subba Rao's story reminds us that scientific progress is a collective effort built on the shoulders of many individuals who often go unrecognized. His work on folic acid and the synthesis of anti-cancer drugs laid the foundation for modern cancer treatments, saving countless lives. Yet, as he passed away in relative obscurity, his legacy reminds us that it is not the pursuit of fame and recognition that drives scientific inquiry but rather the pursuit of knowledge and the betterment of society. It is a reminder that even the smallest scientific contributions can have a tremendously impact. We should strive to recognize and honor the often-overlooked



heroes who make these contributions possible. As Louis Pasteur rightly said, “Science knows no country because knowledge belongs to humanity and is the torch which illuminates the world.”

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References

- Bhargava, P. M. (2001). Dr. Yellapragada Subba Row (1895–1948): He transformed science; changed lives. *Journal, Indian Academy of Clinical Medicine*, 2(1–2), 96–100.
- Bharti, A. H., & Marfatia, Y. S. (2017). Yellapragada Subba Row, the unsung Indian biochemist behind methotrexate and other drugs. *Indian Journal of Dermatology, Venereology, and Leprology*, 83(6), 733–735. https://doi.org/10.4103/ijdvl.IJDVL_1018_16
- Farber, S., Diamond, L. K., Mercer, R. D., Sylvester, R. F., & Wolff, J. A. (1948). Temporary remissions in acute leukemia in children produced by folic acid antagonist, 4-aminopteroyl-glutamic acid (aminopterin). *New England Journal of Medicine*, 238, 787–793.
- Fiske, C. H., & Subbarao, Y. (1925). The colorimetric determination of phosphorus. *Journal of Biological Chemistry*, 66(2), 375–400. [https://doi.org/10.1016/S0021-9258\(18\)84756-1](https://doi.org/10.1016/S0021-9258(18)84756-1)
- Fiske, C. H., & Subbarow, Y. (1928). The isolation and function of phosphocreatine. *Science*, 67(1728), 169–170. <https://doi.org/10.1126/science.67.1728.169>
- Fiske, C. H., & Subbarow, Y. (1929). Phosphorus compounds of muscle and liver. *Science*, 70(1816), 381–382. <https://doi.org/10.1126/science.70.1816.381.b>
- Gupta, S. P. (1976). An Indian scientist in America: The story of Dr. Yellapragada Subba Row. *Bulletin of the Indian Institute of History of Medicine*, 6(2), 128–143.
- Gupta, S. P., Bansal, S., & Ramesh, V. (2013). Remembering Yellapragada SubbaRow. *International Journal of Dermatology*, 52(7), 882–886. <https://doi.org/10.1111/ijd.12075>
- Gupta, S. P. K., & Milford, E. L. (1987). *In quest of panacea: Successes and failures of Yellapragada SubbaRow*. Evelyn Publishers.
- Hewitt, R. L., White, E., & Subbarow, Y. (1947). Experimental chemotherapy of filariasis; effect of piperazine derivatives against naturally acquired filarial infections in cotton rats and dogs. *The Journal of Laboratory and Clinical Medicine*, 32(11), 1304–1313.
- Mckenzie, D., & Stadler, M. (1948). The use of synthetic medium as an in vitro test of possible chemotherapeutic agents against gram-negative bacteria. *Journal of Immunology*, 60(2), 283–294.
- Narasimhan, R. (2003). *Yellapragada Subbarow: A life in quest of panacea*. Vigyan Prasar.
- Subbarow, Y., Dann, W. J., & Meilman, E. (1938). The effect of β -aminopyridine in experimental blacktongue. *Journal of the American Chemical Society*, 60(6), 1510–1511.
- Subbarow, Y., Hastings, A. B., & Elkin, M. (1945). Chemistry of anti-pernicious anemia substances of liver. *Vitamins & Hormones*, 3, 237–296.

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