

ERROR OR FRAUD IN SCIENCE: AUXINS A AND B AND ANIMAL TUMOR PROTEINS

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Abstract: Erroneous reports of plant growth regulators auxins a and b and of D-amino acids in animal tumor proteins have led to allegations of fraud against the chemist Hanni Erxleben. Biographical information not previously available concerning her is presented and these cases discussed in its connection. Also considered are numerous other cases of error from the same laboratory. It is concluded that the way that laboratory was managed made fraud possible, perhaps even likely.

Key Words: auxin a; auxin b; D-amino acids; Erxleben; Kögl; laboratory management; tumor proteins.

INTRODUCTION

As Wildman (1997) has described in detail, three workers at the University of Utrecht in the Netherlands, Fritz Kögl, Arie Jan Haagen-Smit, and Hanni Erxleben, reported in the 1930s on two plant growth regulating substances, auxins a and b. Kögl was the professor and principal investigator, Haagen-Smit and Erxleben his assistants. They described the isolation and the chemical characterization of the two substances in an extensive series of publications. Haagen-Smit performed the initial isolations and monitoring by bioassay, and Erxleben did the work of structural characterization of the products. Unfortunately, auxins a and b were later shown to be non-existent. It must be mentioned, however, that to their credit these workers, simultaneously and separately with Kenneth Thimann and Joseph Koepfli, also identified indoleacetic acid as a plant auxin. This multiple discovery (Troyer 1992) revolutionized the study of plant growth regulation and led to numerous applications in agriculture and other practical plant sciences. Kögl and Erxleben later, beginning in 1939, reported the sensational and controversial finding that animal tumor proteins contain large amounts of unnatural D-amino acids. This claim was never confirmed and has, in fact, been judged to have been erroneous (Miller 1950; Stroud and Smith 1984). A number of writers over the years have alleged that these reports from Kögl's laboratory concerning auxins and tumor proteins involved not simply error, but outright fraud on the part of Erxleben.

Biographies exist for Kögl (1897–1959) (Lynen 1959; van der Kerk 1959; Borg 1959a, 1959b; Havinga 1960; Snelders 1994) as well as for Haagen-Smit (1900–1977) (Anonymous 1966; Pitts and Stephens 1978; Bonner 1979, 1989; Cooke 1999). Until now, however, such information concerning Erxleben has not been publicly available. The purpose of this communication is twofold: to provide details of Erxleben's life, and in their light to review the question of fraud or error in the two cases mentioned.

LIFE OF ERXLEBEN (1903–2001)

Details of the life of Johanne Wilhelmine (Hanni) Erxleben through the year 1930 are to be found in biographical summaries that she wrote (Erxleben 1923, 1931) and in information from the state archives of Bremen, Germany (Hannover 1991a, 1991b). The daughter of a musician, Karl Erxleben, she was born in Bremen 22 June 1903 and baptized Evangelical Lutheran. She attended schools in Bremen from 1910 to 1924: the *Volksschule am Geschwarenenweg* (an elementary school) from 1910 to 1913; the *Waetge Schule* (a private girls' school) from 1913 to 1916; the *Gymnasium an der Kleinen Helle* (a municipal lyceum) from 1916 to 1923; and the *Oberlyzeum von A. Kipfenberg* (a municipal training school for teachers) from 1923 to 1924. Her career objective was to become a school teacher. She then worked as a private governess until 1926, when she began to study chemistry at the University of Göttingen.

She was supported by a student-aid stipend while at Göttingen and supplemented her income by working during vacations as a helper and substitute in the Bremen schools. She passed the first chemistry examination in 1928, and that year studied for one term at the *Technische Hochschule* (technical university) in Munich. Having then re-matriculated at Göttingen, she passed the second chemistry examination in 1929 and began work on her doctorate in the *Allgemeine Chemische Institut* (General Chemistry Institute), pursuing research under the direction of Kögl. She completed this work in 1930 and passed the final examination on 17 December of that year, presenting a dissertation on the chemistry of certain mushroom constituents (Erxleben 1931).

Kögl meanwhile in 1930 had assumed duties as Ordinary Professor of Organic and Propadeutic Chemistry at the University of Utrecht, and upon Erxleben's completion of the doctorate brought her there to serve as his assistant. According to the records at Utrecht (Tromp 1990) she took up that position 1 January 1931. Later, after Haagen-Smit emigrated to the United

States, she was promoted as of 1 October 1936 to the rank of head assistant which he had held. She became a naturalized Dutch citizen in 1938 (Kögl 1952) and was named *privaat-docent* on 8 June 1939, with authorization to lecture on newer methods of organic chemistry. It was during this stay at Utrecht that the principal work on auxins a and b and tumor proteins was carried out.

World War II and the German occupation of the Netherlands from 1940 to 1945 brought difficult times to the people of the organic chemistry laboratory at Utrecht, as to the country as a whole. Jews were rounded up and deported, universities were restricted or closed, and students were subjected to a labor draft to work in Germany (Warmbrunn 1963). Many such students went into hiding, becoming *onderduikers* ("divers"). Erxleben was visiting her father in Bremen at the time of the invasion (Kögl 1952), a circumstance which raised suspicion in the eyes of her Dutch associates. She did, in fact, openly display Nazi sympathies during the occupation, fraternizing with German army officers and members of the NSB (*Nationaal-Socialistische Beweging*), Dutch Nazis (van Kolfchooten 1993; Wildman 1997). Indeed, Thimann (1990), although pointing out that it was hearsay, stated that she was said to have married a German soldier, and Salisbury (1998) without citing any authority even claimed that she was a German spy.

Bloch (1988) reported that after the war Erxleben "disappeared without leaving a trace." As a matter of fact, when the end of the war seemed imminent by 1944, she determined to return to Germany and pursue the career as a school teacher for which she had originally prepared years before (Kögl 1952). She regained her German citizenship in February 1944 (Hannover 1991b), resigning her post in Utrecht as of 1 September 1944 (Tromp 1990), and departed a few days later on 5 September. On that day, known to the Dutch as *Dolle Dinsdag* (Mad Tuesday), she joined masses of Dutch and German Nazis fleeing the country for safety from the advancing Allied armies (Maas 1970).

Little is known of her activities during the years 1944 to 1946, only that she was in the Russian-occupied zone where she endured many miseries (Kögl 1952). She eventually made her way to Bremen, arriving there in 1946 from the village of Keula in East Germany (Hannover 1991b).

Information concerning Erxleben's subsequent career in the schools of Germany comes from the Bremen state archives and from one of her friends (Hannover 1991a, 1991b; Vogel 1991). She served as a teacher in the Bremen school where she had been a pupil 30 years before, the *Gymnasium an der Kleinen Helle*, from 1946 to 1952. Kögl (1952) in the latter year invited her to return to Utrecht temporarily for six months to teach analytical techniques to his young assistants. She

declined, however, because she had just been offered a position as headmistress of another school, the *Bavinck-Gymnasium* in Bielefeld (now known as the *Gymnasium am Waldhof*). She served in that post until 1962 and was highly regarded as an energetic and successful school director. She was then appointed as an *Oberschulrätin* (government inspector of secondary schools) in Münster, serving there until 1966 when she retired in Bielefeld.

She was the featured principal speaker in September 1966 on the occasion of the 50th jubilee of her old school in Bremen, a four-day celebratory event (Erxleben 1966). During a long retirement she remained active in movements for protection of the environment and of animals. She was a co-founder in 1975 of the *Bund für Tier- und Naturschutz* (Alliance for the Protection of Animals and Nature), an organization still active today. She died in Bielefeld in 2001.

ERROR OR FRAUD

Eventually it became clear that the reports from Kögl's laboratory mentioned earlier were erroneous. With respect to auxins a and b (Wildman 1997), no other workers could repeat the isolations; they found only indoleacetic acid in urine and other sources. Also, later examination of supposedly purified original samples of the auxins and their derivatives showed them to be totally different from what was claimed. As for D-amino acids from tumor proteins, numerous other workers tried to confirm the results, but failed. Likewise original amino acid samples were found by later analysis to be highly impure and contaminated (van Kolfchooten 1993). Referring to this situation, Havinga (1960) stated that "...Erxlebens experimentele resultaten niet juist konden zijn geweest" (Erxleben's experimental results could not have been correct). Snelders (1994) went no further, stating that Erxleben's experiments "*weinig betrouwbare resultaten hadden opgeleverd*" (had yielded few reliable results) and that the tumor reports "*...gebaseerd waren op jaarenlang onjuist wetenschappelijk onderzoek*" (were based on years-long incorrect scientific research). These two authors, in other words, described the case as simply one of error or ineptitude.

A number of other writers have accused Erxleben of fraud without, however, citing any basis for this allegation: "...eine langjährige Mitarbeiterin wissenschaftlichen Resultate gefälscht hat" (a female co-worker of many years falsified scientific results) (Lynen 1959); "the published results were simply fabricated" (Levitt 1974); "Both discoveries proved to be fabrications" (Bloch 1987); "Auxin a and auxin b were fabrications apparently invented by Hanni Erxleben" (Bonner 1994). Haagen-Smit in a letter quoted by Jacobs (1979), by Bonner (1989), and by Wildman

(1997) referred to Erxleben's "error" and her "persistence in covering up," but did not offer any further explanation or evidence for such accusations.

Still other authors cited only evidence of error as support for the charge of fraud: the work was not repeatable or the auxin samples were wrong (Karlson 1982, 1986; Bloch 1988; Mori, Kamada, and Kido 1991). Bloch, without citing any source for the assertion, attributed Erxleben's motive to unrequited amorous attraction. The discussion of Schnepf (2002) was based on those of other authors mentioned. Only Buffel (1985) was unconvinced, maintaining that "any insinuation of either ignorance or fraud cannot be taken seriously."

One additional report is more disturbing. Workers in the laboratory of Hans Fischer had been unable to repeat the tumor protein results. When Erxleben visited Fischer's laboratory in 1944 and participated in repetition of the work there, however, the claimed results were confirmed (Kögl 1949). Fischer later concluded that he "had been fooled by Kögl's assistant" (Bucher 1983). Perhaps on this basis Karlson (1986) asserted that Erxleben probably enriched her preparations by adding pure D-glutamic acid, of which she had a plentiful supply for comparison purposes.

The authors cited who accused Erxleben of fraud include Nobel Prize winners, members of the National Academy of Sciences, and other distinguished scientists. Their testimony is not to be taken lightly. Yet none of them, except for Haagen-Smit, had any direct involvement in the laboratory at Utrecht. They were not eyewitnesses, so their opinions must have been based not only on the public record but also on what they heard from others. Scientists in a field communicate among themselves not just through formal publication but in addition by word-of-mouth discussion, especially when judging the quality or validity of the work of others. To what extent such grapevine knowledge may have played a role in this case is uncertain since they naturally did not cite it. An exception is van Kolschooten (1993), who based his account on well-cited interviews of former students and associates of Kögl.

Wildman (1997) after analyzing the auxin case extensively remained puzzled. He was left with "a feeling that Kögl and Haagen-Smit were not entirely innocent victims," and the idea that Erxleben faked everything was for him "too simple a rationalization." Here it might be noted that Haagen-Smit emigrated to the United States in 1936, and from about 1937 attempts to extract auxin from urine no longer succeeded in Kögl's own laboratory (Buffel 1985). Jacobs (quoted by Wildman 1997) later also expressed doubt, stating that he "was suspicious of the way in which blame was so summarily dumped on the *female* lab technician" and didn't like "The *woman* did it attitude."

None of the authors cited here refer to the interesting fact that at least nine other cases of invalid results, some of them grossly so, were published by Kögl during the same period as the two considered. Erxleben participated in a major way in only two of these and contributed slightly to only two others. Fifteen other coworkers and associates of Kögl were involved in these cases, yet no allegations of fraud have been leveled at any of them.

The vitamin biotin was isolated and named, but it was incorrectly maintained that there were two forms of the substance and erroneous structural data were published (György 1954). Incorrect structures were also reported for the mushroom constituent muscarine based on highly contaminated products (Wilkinson 1961). (It should be noted that years later workers in Kögl's laboratory produced the correct structure and synthesized the substance.) Incorrect structures were also described for the quinones perezone, perezinone, and alpha- and beta-pipitzols (Thomson 1971).

Three studies of fungus constituents involved reported results just as invalid as those of the auxins and tumor proteins and caused considerable confusion (Gill and Steglich 1987). The structure of telephoric acid was reported from examination of degradation products to be that of a phenanthraquinone. Later workers in several laboratories, however, found completely different results and determined the structure to be that of a benzofuranquinone. A red pigment called "muscarufin" was said to have been isolated from an agaric mushroom, but later workers could not repeat the isolation and such a pigment was found to be non-existent (Musso 1979). It was also claimed that "boletol," a substance said to be responsible for a blue color reaction in the bruised flesh of certain mushrooms, was isolated in pure form, its structure determined, and that structure confirmed by synthesis. Later workers showed that in fact the actual bluing agents were several completely different compounds, the synthetic product did not show the bluing reaction, and original samples from Utrecht were impure mixtures which also did not show the color reaction (Bräm and Eugster 1969).

A number of persons were involved in these numerous errors. Why was only Erxleben singled out for charges of fraud? When he examined Wildman's (1997) analysis of the auxin case, Sabbagh (1999) laid emphasis on the human aspects of science which existed in this situation: "ambition, haste to publish, threats to sue, political smears, reluctance to admit error, even sex." Erxleben was disliked, even despised, by her Dutch associates, largely because of her then Nazi sympathies but also because of her perceived attitude and behavior toward subordinate personnel; they mockingly referred to her as "*Frau Direktorin*" (Madame Director) (van Kolschooten 1993). Their respect for Kögl, on the other hand, was too great for him to be openly doubted.

Kögl, unlike Erxleben, detested Naziism and during the wartime German occupation remained steadfastly loyal to his adopted country, once declining the offer of a prestigious professorship at the University of Berlin. According to his daughter (Kögl 2000) he also engaged in illegal activities which could have exposed him to serious danger. He regularly listened to British broadcasts on a hidden radio. He allowed coworker and student “divers” to hide from the German authorities in the cellars of his laboratory building, bringing food and supplies to them by bicycle. The Dutch resistance group in Utrecht during this time maintained a careful watch so that no harm would come to him. After the war he not only retained his professorship but also was named *Ridder* (Knight) in the *Orde van de Nederlandse Leeuw* (Order of the Netherlands Lion), a high honor indeed.

Kögl got widespread scientific acclaim during the 1930s and a number of awards, including the German Emil Fischer Medal in 1933, the Swedish Scheele Medal in 1936, and a resolution of recognition from the American Society of Plant Physiologists in 1937 (Harvey and Loehwing 1937). He received 17 nominations for the Nobel Prize in chemistry by 13 different persons, including six previous or later winners, but was never awarded it (Crawford, Heilbron, and Ullrich 1987).

How could so many instances of totally invalid scientific results emanate from the laboratory of one whom many regarded as brilliant and worthy of a Nobel prize? The instances are numerous enough to raise questions concerning his management style. He did no laboratory work himself after assuming his professorship, instead depending on the efforts of students and assistants (Thimann 1960). “He always put his name first on the papers” yet “had very little to do with it” (Thimann, quoted by Wildman 1997). According to Haagen-Smit (Thimann 1991), his procedure was to work most of the day in his office, on the door of which was a signal light: if it shone red, he was not to be disturbed; if it was white, it was permitted to knock (Rietsema 1991). Then near the end of the day he would go to the laboratories to ask what had been done that day. As one of his students put it (Van Deenen n.d.), he “passed by on his daily afternoon visits to his coworkers—striding as a general to inspect the troops”, a not very close oversight.

Kögl was by all accounts the *Herr Professor*, stern, exacting, and not to be questioned or contradicted. Haagen-Smit in the letter previously mentioned referred to his “dictatorial behavior” and his “eagerness to publish,” qualities which would have made it difficult for error to be acknowledged, let alone publicly retracted. Barinaga (1991) considered that laboratory management style was related to the possibility of fraud, and Lodisch (1982), discussing the responsibilities of the principal investigator in science, pointed out that the

farther one is from day-to-day activities of the laboratory, the more likely is fraud in a subordinate. Further, when fraudulent work is published, the principal investigator must bear a large responsibility for it. Dutch workers after Kögl’s death spoke with great reserve about his contributions to chemistry (van Kolschooten 1993), a reserve prompted by “*et angstige vermoeden dat er iets heel erg scheef heeft gezeten in het lab voor organische chemie*” (the fearful suspicion that something quite evilly false had sat in the lab for organic chemistry). But they could not bring themselves to criticize Kögl or Haagen-Smit, only Erxleben. Whether there was fraud on her part there was certainly ineptitude, and on that of Kögl as principal investigator there was certainly error in the form of poor scientific judgment.

CONCLUSION

Of the numerous invalid scientific results published from Fritz Kögl’s organic chemistry laboratory in the 1930s and 1940s, only two cases have evoked accusations of fraud, and only the German Hanni Erxleben has been named as a perpetrator; none of her Dutch associates have been so charged. Her accusers have offered no ironclad or eye-witness proof of such fraud, only strong circumstantial evidence. If she did commit it, the atmosphere and management of the laboratory by Kögl made it possible, perhaps even likely. Whatever the truth, she eventually washed her hands of chemical research and pursued a new and different course with a distinguished career as an educator. Years later in writing of Germany, her country, she might well have been describing her own two-fold life (Erxleben 1966): “*Die seelische Druck der Nazizeit und die Schrecken des totalen Krieges waren überwunden, man stand zwar vor Trümmern aber gleichzeitig vor einem Neubeginn und glaubte, dass all die bitteren Erfahrungen der Vergangenheit nun fruchtbar werden könnten, um eine neue und bessere Zukunft aufzubauen*” (The psychic pressure of the Nazi era and the horrors of total war were overcome, one stood indeed before ruins but at the same time before a new beginning and believed that all the bitter experiences of the past could now become fruitful in order to build up a new and better future).

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