The Rosy Periwinkle: The Fact and the Fiction Behind the Development of Vinca Drugs

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Agenda

• History and early research

• Development of vinca alkaloids for treatment of cancer

• Claims of “biopiracy”

• How would such a discovery be treated today?

• Conclusions
Medical History of the Periwinkle

• Vinca species are widespread, widely referenced, and their uses have been publicized for centuries:

  • AD 77-79: Pliny the Elder, in *Naturalis Historiae*

  • 14th Century: Chaucer, references to “parwynke”

  • 1480: Apuleius’s *Herbarium*, as a treatment for “devil sickness and demoniacal possessions”

  • 1552: Macer’s *Herbal*, to counter “wykked spirytis”

  • 1657: William Coles’ *Adam in Eden* describes its use for wounds and other inflammatory conditions
South African Medical Record, Cape Town
24: 1-24 (Jan. 9) 1926
* Tannins as Intestinal Astringents. J. W. C. Gunn.—p. 11.

24: 25-46 (Jan. 23) 1926
Roentgen-Ray Therapy. F. W. Weber.—p. 27.
Two Cases of Partial Gastrectomy. R. L. Daly.—p. 38.
Continued Interest in Vincas for Diabetes

CURRENT MEDICAL LITERATURE

Medical J. Australia, Sydney

2: 577-610 (Nov. 10) 1928

History of Spectacles. E. T. Smith.—p. 578.
Chinosol Treatment of "Simple" Ulcerative Colitis. B. Corkill.—p. 589.
Four Interesting Jaw Tumors. P. Pickerill.—p. 591.

2: 611-638 (Nov. 17) 1928

*Use of Morphine in Eclampsia. A. M. Davidson.—p. 612.
*Microscope Slide Precipitation Test for Syphilis. T. Hamilton.—p. 621.
Vinca Treatment of Diabetes.—*Vinca* is a perennial plant which grows plentifully in the coastal districts of Queensland from Moreton Bay to Thursday Island. The species of the genus *Vinca* are commonly known as periwinkle. It belongs to the natural order *Apocynaceae*. The flowers are sometimes pink, *Vinca rosea*, and sometimes white, *Vinca alba*. It appears that this plant was first used as a remedy for diabetes in Africa and in Queensland; today a great number of persons are taking it daily in the belief that they are benefited by its use. Three alkaloids have been isolated from *Vinca rosea*. Nye and Fitzgerald have also prepared a tincture with which most of their experiments have been made. They have carried out tests on five patients, in all of whom the results of treatment were uniformly unsatisfactory. The vinca treatment had no appreciable effect on the fasting blood sugar nor did it diminish the rise of the curve after dextrose. The beneficial effect felt by the patients who are so confident of its results is possibly due to the fact that the preparation has a weak digitalis-like action in common with other members of the *Apocynaceae*.
Vinca Extracts for Treatment of Cancer: Key Facts

• Research was conducted in 1950’s

• Two research groups working simultaneously in the late 50’s
  - U. Western Ontario (Canada) scientists investigating anti-diabetic properties
  - Lilly scientists screening more widely for endocrine, oncology, neuroscience, antimicrobial, antiviral, or insecticidal properties
    - All extracts subject to the same screens, “regardless of medical claims found in the literature.”

• Sources of vinca plant material
  - Evidence suggests Western Ontario team received first sample from Jamaica.
  - Lilly received first sample from commercial biological supplier, and plant material for commercialized product was sourced worldwide from any available supplier.
  - To ensure constant supply, plants were eventually sourced from commercial growers in Texas, United States.
Clinical Uses

• Velban® (vinblastine sulfate)
  • Approved 1961
  • Indications: Hodgkin’s disease and treatment-resistant choriocarcinoma

• Oncovin® (vincristine sulfate)
  • Approved 1963
  • Indications: acute childhood leukemia
“Famous Case” of What? Successful Scientific Research Efforts
How Would Development of Vincas Be Treated under WIPO IGC Draft Articles?

• Does this meet the definition of “Traditional Knowledge?”
  • No evidence to suggest distinctive association with or use by an “indigenous” or “local” community, or to demonstrate intergenerational transmission of traditional knowledge (TK)
  • Who bears the burden to prove TK was or was not used in the invention?

• Who would have the right to claim a “share of the benefits?”
  • Madagascar? Jamaica? South Africa? Australia? What about Italy or the UK?
  • No clear association with an indigenous group; does the state claim the benefits?

• Exceptions for independent invention?
  • What if Jamaica acknowledges the invention arose independently through information obtained from printed publications, but Madagascar continues to demand benefits (despite no credible evidence TK existed or was in continuous use in Madagascar)?
Under the Nagoya Protocol to the Convention on Biological Diversity?

- Who receives benefits under the Nagoya Protocol?
  - Under Article 10, a Global Multilateral Benefit-sharing Mechanism is to be considered for benefits arising from GR/TK in “transboundary” situations or when prior informed consent cannot be obtained
    - But any benefits shared would go to conservation of biological diversity and sustainable use of its components globally, not to providers
  - Under Article 11, States that share the same GR or TK should cooperate to ensure benefit-sharing under the Protocol

- How does this comport with benefit-sharing under the WIPO draft articles for protection of GR/TK?
  - Do benefits flow to the Global Multilateral Benefit-sharing Mechanism, the indigenous or local community from which GR/TK was accessed, … or any entity that makes a claim?
Would These Drugs Even Have Been Developed Today?

• Would samples have been available for biological tests?
  • Many countries have no national laws governing ABS
  • Recent Lilly attempts to secure an ABS agreement with Cameroon failed for this very reason

• This should create an incentive to implement national laws that facilitate new discoveries
  • If Jamaica has no ABS regulations, or South Africa has burdensome regulations, why not enter into ABS agreement with Australia, where vinca is plentiful?

• Would the risk of patent revocation, combined with uncertainty over benefit-sharing requirements, ensure no product would be developed?
Housewife Writes Thanks For New Anticancer Item

Have you ever wondered how the product you researched, developed, manufactured, packaged, or shipped served a patient. A housewife in Menomonee Falls, Wisconsin, whose husband has been treated with some of the company’s new anticancer products describes the results they had for her husband.

“The three years ago my husband had extensive surgery for a neoplasm in the bronchus, left lung, and extending slightly onto the lower lobe of the right lung. We were and are thoroughly familiar with the high mortality rate for this type of cancer, and we experienced all the sorrow, dread and terror usually associated with this disease. At that time, my husband had the usual physical therapy, drug therapy, etc. I will admit that this therapy is very expensive; however, I have not begrudged too much the expense.

“When I stopped in our drug store yesterday, the druggist asked how Bill was getting along, and I told him the truth—that Bill looks, acts, and feels better than he has for 15 years. That’s when the druggist made the startling statement. He said, ‘You can thank Eli Lilly for that.’

“So I do. I thank you from the bottom of my heart.

“You see, Bill’s just an ordinary man, doing an ordinary job. But he means everything to me and to our children. I thank you for the three years we have had, and for the years that we will have in the future. The children thank you for letting them have a father during their teen years. We are all aware that this might not be permanent, but the years you have given us are sincerely appreciated.

“I thank you, Eli Lilly. And I ask that you extend our appreciation to everyone in your organization who has made this possible.”
Conclusions

• Interest in periwinkle was driven by peer-reviewed, published research – not anecdotes, not TK

• There is no evidence of TK relating to use of periwinkle to treat cancer
  – Pliny’s writings would not constitute TK under WIPO Draft Articles

• Natural product R&D is already highly risky and complex
  – The path of uncertainty and controversy will be avoided

• Greater uncertainty under WIPO and Nagoya Protocol creates risk that any patented product may be subject to claims of “biopiracy”

• Industry wants to comply with CBD obligations on ABS, but we must have legal certainty
Spiderman is from Ghana

2000 patents per year are granted on Indian TK

If I ‘google’ “biopiracy,” I get over 1000 hits