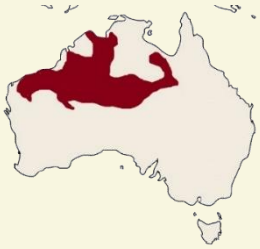
Nicotiana benthamiana

A native Australian tobacco now used in the production of a Covid-19 vaccine

Widespread across north-western Australia is a modest, easily overlooked herbaceous plant, *Nicotiana benthamiana*. For all that, scientifically, it is without doubt Australia's most famous native plant. It is extremely susceptible to plant pathogens, and for this reason has been used extensively in scientific research on the mechanisms of disease in crops. Like commercial tobacco, it is amenable to the expression of foreign genes (genetic engineering) and thus ideal for the development of human vaccines, including Covid-19.

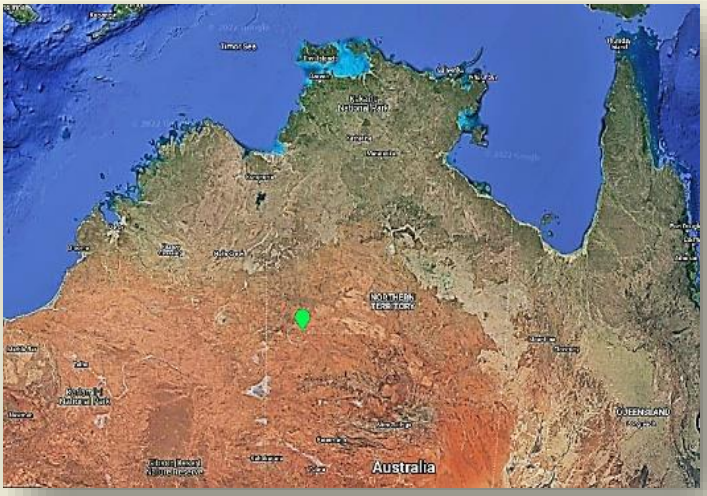


The generic name, *Nicotiana*, reflects its close taxonomic relationship to *Nicotiana tabacum* (common tobacco). *Nicotiana tabacum* is native to the Caribbean but there are perhaps 60 - 70 *Nicotiana* species worldwide, many from South America. Australia has 21 endemic species and one naturalised species.

Indigenous Australians have long used the native tobacco, *N. benthamiana,* as a stimulant as it contains high levels of nicotine and other alkaloids. During the 1837 voyage of HMS Beagle to survey the Australian coastline, specimens of *N. benthamiana* were collected by the ship's surgeon Benjamin Bynoe. However, the location was rather imprecise, simply recorded as *N. W. coast of New Holland* (Australia).

***Nicotiana benthamiana* –**
Photo: Richard O'Brien

This native tobacco has long been recognised as a *model plant*, studied intensively because of the extreme susceptibility of a single lineage to viral infections, leading to discoveries relating to viral infections in plants and more recently, and relevantly, vaccine production. (Model plants are species chosen for particular characteristics



The original seed of the *laboratory* strain of *Nicotiana benthamiana* is believed to have been collected near the Granites gold mine in the Tanami Desert of the Northern Territory – an extreme environment indeed! Centre for Tropical Crops and Image: Biocommodities, Queensland University of Technology: https://sefapps02.qut.edu.au/biology/isolatesmap.php

that facilitate the investigation of the general principles and mechanisms of physiology, biochemistry, ecology, evolution, genetics. Most importantly, a handful of often-obscure plant species have been used widely in recent decades to explore biotechnological innovations in agriculture).

As for disease, its importance as a research tool is because of a *loss of function* mutation (72-bp insertion in the RNA-dependent polymerase gene) in a particular gene *Rdr1*, making it hypersusceptible to viruses.

Although the species is widespread across northern Australia where it grows amongst rocks on cliffs and hills, the origins of the lineage used for laboratory studies have been found in only a very few locations, namely the Judbarra Gregory River and the Fish River in the Northern Territory. Seed of the now famous *laboratory* strain seems to have been collected in 1936 near the Granites Gold Mine in the Tanami Desert of the Northern Territory by Professor Cleland of the Waite Institute Campus of the University of Adelaide. The seed was sent in 1939 to botanist Professor T H Goodspeed, who was director of the University of California Botanical Garden from 1919 to 1957.

You might ask whether this mutation confers an advantage in the natural habitat. This early strain is believed to have appeared ~ 0.8 million years ago in the extreme heat and aridity of central Australia, where defences against viral, bacterial and fungal diseases were foregone to achieve opportunistic rapid early growth and production of hundreds of tiny seeds as a means of survival. These characteristics are apparently not as obvious in plants that evolved under more benign conditions. The mutant form is therefore recognised as an *extremophile*, an organism able to survive in extreme environments that can include extreme temperature, salinity, pH level or radiation.

Nicotiana benthamiana – Photo: Richard O'Brien

It is now of such interest for its use in the production of an anti-Covid-19 vaccine. A Canadian biotechnology company *Medicago Inc.*, is using plants of *N. benthamiana* to produce *virus-like particles* over a short period of time and in high volumes, to enable the rapid production of a Covid-19 vaccine. CoVLP is a COVID-19 vaccine candidate; it is a coronavirus *virus-like particle* developed by Medicago and GlaxoSmithKline and expressed ectopically by *Nicotiana benthamiana*. The technique of *molecular farming* is low cost, fast and safe and by September 2021, Phase II-III trials of the vaccine had been started in North America, Latin America and Europe. In December 2021, the companies reported a preliminary analysis that showed an efficiency of 75% against the Delta variant of Covid-19. The term *virus-like particle* vaccine is used to describe a molecular complex that *resembles* a virus, but it *isn't* infectious because it doesn't contain any genetic material of the virus.

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Centre for Tropical Crops and Biocommodities, Queensland University of Technology: *Nicotiana benthamiana*, Genome & Transcriptome, https://benthgenome.qut.edu.au/

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Electronic Flora of South Australia: *Nicotiana benthamiana* fact sheet http://www.flora.sa.gov.au/efsa/lucid/Solanaceae/Solanaceae%20species/key/Australian%20Solanaceae%20species/Media/Html/Nicotiana.htm

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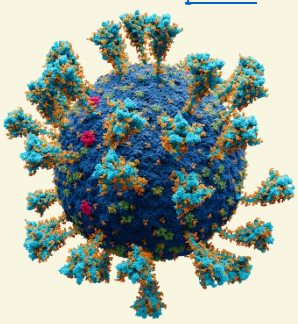
Wikipedia: https://en.wikipedia.org/wiki/CoVLP

Map of distribution adapted from *Atlas of Living Australia*: https://biocache.ala.org.au/occurrences/search?q=lsid:https://id.biodiversity.org.au/node/apni/2912121#tab_mapView



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