



The Historical Use of Medicinal Herbs containing Pyrrolizidine Alkaloids

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Containing Pyrrolizidine Alkaloids

The Historical Record

- Examining the historical record can provide evidence of how herbs were traditionally used. We can follow the route of a herb through history from ancient into modern times to establish longevity of traditional use and whether or not any safety concerns were raised by practitioners in the past.
- Let us consider 3 herbs containing Pyrrolizidine alkaloids which are still in common use – *Symphytum officinale* (Comfrey), *Borago officinalis* (Borage) and *Tussilago farfara* (Coltsfoot) which have been traditionally used in Western Herbal Medicine for centuries.
- This can provide insight into other herbs such as *Petasites hybridus* (Butterbur), *Mysotis arvensis* (Forget-Me-Not) or *Eupatorium perfoliatum* (Boneset) and other species which are now less commonly used.

Issues with Historical Records

- While there are several ancient herbal texts, very few can be said to be critical editions. A critical edition is based on a comparison of extant manuscripts and a translation of the resulting best version.
- There is a need to refine our study to those scholars with wide-ranging influence over long periods of time who critiqued earlier commentary to demonstrate practice-based continuity of use.
- We need to consider the historical timeframe. While long term historical use cannot confirm safety, it does offer scholarly opinion and empirical evidence about the use of herbs in general.
- Another issue is identification. We must be clear that the plants the ancients referred to are the very same plants under consideration?

The Classical Scholars

- **Pliny the Elder** (23-79 CE)
- **Dioscorides** (40-90 CE)
- **Pseudo-Apuleius** (124-170 CE)
- **Galen** (130-210 CE)
- **Paulus Aegineta** (625-690)
- **Avicenna** (980-1037 CE)
- **Abenguefit** (997-1074)



Salerno & Montpellier

- Much of the knowledge of these classical scholars (and others of the Graeco-Arabic tradition) were consolidated at early medical schools such as Salerno and Montpellier, especially between the 10th and 12th century. Scholars from across Europe would study a particular text attributed to **Matthaeus Platearius** known as the *Circa Instans*. This textbook was translated and copied by hand. The text was widely used across Europe and can offer a glimpse into common usages during this period.

seymes pour faire les cheueux
jaunes



Bastard est chault
et sec en chiere de grece.
C'est le barbel de grece on
fait les bonnes herbes
minces on en tiennent au
bois en grant quantite
il aboite d'aucune et
de polubine. **C**ontre
pocripse au royaume
pour faire de chertie de la
barbe de bust de poige
de frouit de perzel auer
mel pousant et pour
comme aloie. Elle vault
aussi comme la d'oste de
la rate. **C**est un aneste
diffuse et strangurie.

Ce peut ampephement de
vaine. Et romme y haque passio
poudre faite de la semelle
de bust de semence d'ame
et de frouit auer auer de
frouit et que on en pousse
une nulliere a l'ung auer de
blant mais se le parant a
seme donne le auer eue on
my en eane le pousse seures
et le donne. **C**adoulain
et anseure des genitales a la d'ostre et
my bien la raine d'auer
et en fuy amplasse. **C**est
my auer de la pousse on
de la grece ou le fuy d'ame
l'onde ce ote toute anseure.



Ble de septe herbe
d'auver que on appelle
bete les gres l'appellent. **C**est
elle est bonne pour manger
elle est chaulte on pousse.

degre et moult on sevoid
elle avertu de bien nourry
et d'augendres bon sang
en la nuit auer chaz epasse
elle lache m'auver de frouit
le venre. **C**est un aneste
pousse de venre. rause de
seure et de chaulte pour
fuy d'ostre et de celle auer
sel on ote.

et en tout pousse
et en tout



Blatte bisanne. Elles
sont chaultes et seures
on sevoid de degre. et seient
d'auver pousse qui resamble
al'auver. Et est bonne en
la mer et a fuy d'ostre et
neige. Elle est chaulte de
frouit et de moult de frouit.

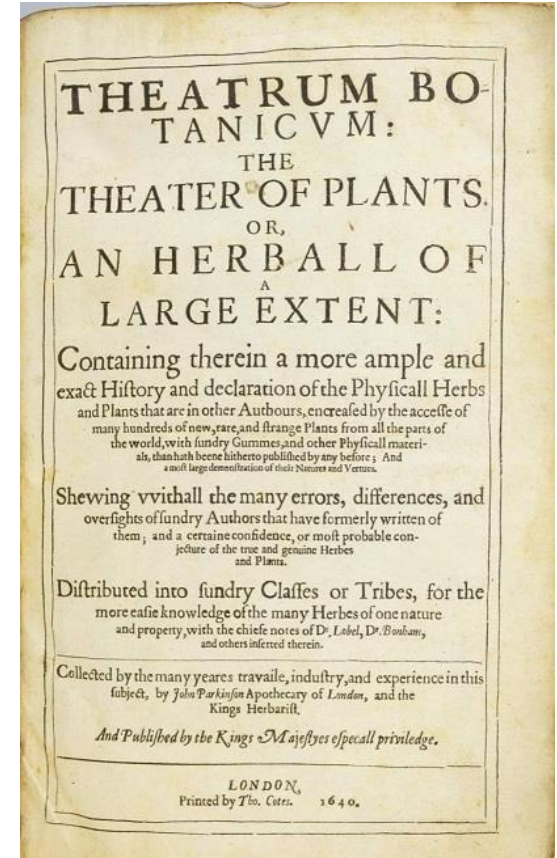


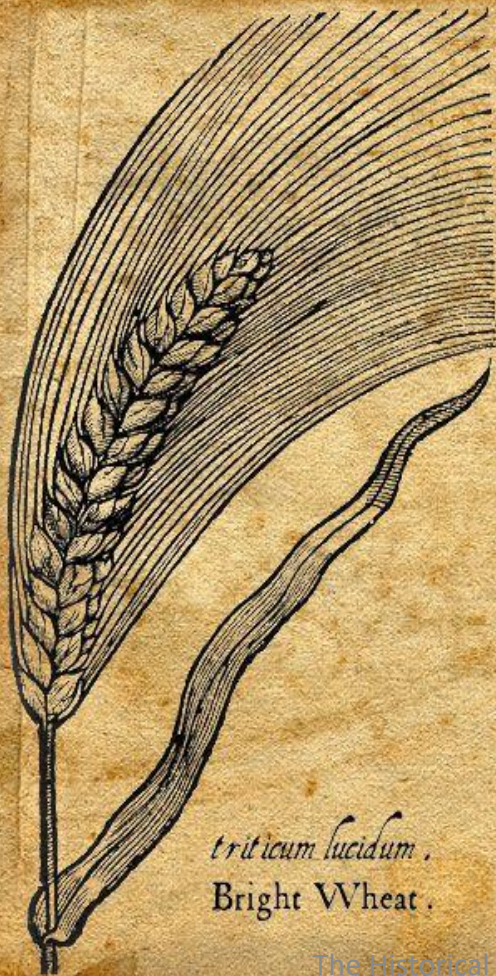
Cest un aneste
Cest un aneste
Cest un aneste
Cest un aneste

xlvi
xlvi
xlvi
xlvi

Early Modern Times

- Tadgh Ó Cuinn (c. 1415)
- William Turner (1509-1568)
- John Parkinson (1567-1650)
- John Gerard (1545-1612)
- Nicholas Culpeper (1616-1654)
- William Salmon (1614-1713)





triticum lucidum.
Bright Wheat.

selections from
THE HERBALL
OR
GENERALL HISTORIE OF PLANTES
*Containing the description, place,
time, names, nature,
&
vertues*
OF ALL SORTS OF HERBES
for meate, medicine or sweet-smelling use, &c.

gathered by
John Gerard
Master of Surgery
LONDON

Enlarged and Amended by
Thomas Johnson
Citizen and Apothecary of London

anno 2008



Velluminous Press

Modern Times

- **Samuel Thompson** (1769-1843)
- **The Physiomedicalists** – William Cook, JM Thurston, Wooster Beach, Albert Coffin
- **The Eclectics** – Finley Ellingwood, John King, Harvey Wilkes Felter, John Scudder, John Uri Lloyd
- **National Association of Medical Herbalists** of Great Britain (1921) *The National Botanic Pharmacopoeia*.
- **Maud Grieve** (1858-1941)

Relevance of Historical Texts

- Recent research has shown that ancient herbals still contain relevant information. For example a recent study examined Dioscorides' recommendations on diuretic herbs and found that almost 60% of them have since been confirmed by modern research. Rather than dismiss the remaining herbs that have not been confirmed the authors suggest they should become the focus of further research ([Yarnell & Touwaide, 2019](#)).



Tussilago farfara L.

- Dioscorides describes the use of coltsfoot smoke inhalations for dry coughs. He also discusses the external use of the leaves for inflammation, and the expulsion of a dead embryo using an internal preparation known as a hydromel, a type of mead (Beck, 2011, p.234).
- Internal use is at least 2000 years old!
- Pliny & Galen also recommend the use of smoke, though curiously Avicenna does not mention the herb at all (Denham, Tobyn & Whitelegg, 2011, p.319).
- In the 14th century Ó Cuinn, echoing common usage in Europe at the time, described Coltsfoot for fever, constipation, and those who have excessive heat, taken internally. The dried leaves were recommended to provoke urine, while fresh leaves were used to move the bowels (Farber, 2010).

- In Medieval France a Coltsfoot leaf painted on a door was the “sign” of an apothecary (Grieve, 1931).
- *Tussilago farfara* (Coltsfoot), once known as ‘British tobacco’, was recommended by some of the earliest known scholars. The English herbalist William Salmon (1644–1713) even referred to it as *coughwort* (Salmon, 1692).

- Culpepper wrote: *“The fresh leaves, or juice, or syrup thereof, is good for a bad dry cough, or wheezing and shortness of breath. The dry leaves are best for those who have their rheums and distillations upon their lungs causing a cough: for which also the dried leaves taken as tobacco or the root is very good. The distilled water hereof simply or with elder-flowers or nightshade is a singularly good remedy against all agues, to drink 2 OZ. at a time and apply cloths wet therein to the head and stomach, which also does much good being applied to any hot swellings or inflammations”*(Poterton, 1983).

Modern Uses of Coltsfoot

- In Russia, Zevin also records similar uses for Coltsfoot but cautions the novice about the pyrrolizidine alkaloid *senkirkine*. He advises a regime of 4 weeks and no more than 2 courses of treatment per annum, indicative of a cautious approach taken as new information was coming into circulation (Zevin, 1997).
- The respected German herbalist Rudolph Weiss writes on the topic “investigations of this kind may be of scientific interest but have no relevance whatsoever to practical therapy ... the amount of the potentially carcinogenic pyrrolizidine alkaloids was so small that it may be disregarded . Weiss also argues against the use of animal experiments to determine toxicity in humans (Weiss, 2001, p.197).

Coltsfoot in Research

- Far from being carcinogenic it has been demonstrated that coltsfoot affects proliferation and apoptosis of human non-small lung cancer cell lines ([Qu et al., 2018](#)).
- Tussilago has also demonstrated apoptosis in human hepatocellular carcinoma lines ([Lee et al., 2014](#)).
- A compound in Coltsfoot called tussilagonone has been found to be hepatoprotective ([Lee et al., 2017](#)).
- There is no systematic research on Tussilago presenting a gap in the literature for further research.



Borago officinalis L.

- *Borago officinalis* (Borage) has a similarly long tradition to Coltsfoot, and is one of the most commonly used herbs in Europe. De Vos (2010) found that traditional European Materia Medica was based on a Dioscoridean tradition that lasted through to the 19th century with remarkably little variation. According to Dioscorides and Pliny, Borage was the famous *Nepenthe* of Homer, which when drunk steeped in wine, brought absolute forgetfulness. (Grieve, 1931).
- *Borage for courage* is a phrase still in use today in WHM (Bartram).

- Paulus of Aeginita confirmed the use of borage as a mood elevator in the 7th century - borage, is frequently mentioned as a herb, which, when eaten, *“imparts gladness to the soul”* (Adams, 1834, p.97).
- The polymath Ibn Sina (c. 980-1037) also mentioned Borage as a mood elevator in his monumental text, the *Canon of Medicine*. The name of the genus is derived from the Arabic *abu araq*, father of sweat, with reference to the plant’s diaphoretic properties.
- The renowned French herbalist Maurice Mességué (1921-2017), whose patients included Winston Churchill, quoted a verse from the famed 11th century School of Salerno: *“When talking of borage this much is clear, that it warms the heart, and it brings good cheer”*. He also referred to Mattioli who prescribed borage for weak hearts, to cool fevers and calm delirium” (Mességué, 1975/1981).

- The botanical historian Maud Grieve recorded several revealing comments on the uses of borage: *“Henslow suggests that the name is derived from barrach, a Celtic word meaning 'a man of courage.'”*
- Gerard says: *“Pliny calls it Euphrosinum, because it maketh a man merry and joyfull: which thing also the old verse concerning Borage doth testifie: Ego Borago - (I, Borage) - Gaudia semper ago. - (Bring alwaies courage.) Those of our time do use the flowers in sallads to exhilerate and make the mind glad. There be also many things made of these used everywhere for the comfort of the heart, for the driving away of sorrow and increasing the joy of the minde. The leaves and floures of Borage put into wine make men and women glad and merry and drive away all sadnesse, dulnesse and melancholy, as Dioscorides and Pliny affirme. Syrup made of the floures of Borage comforteth the heart, purgeth melancholy and quieteth the phrenticke and lunaticke person. The leaves eaten raw ingender good bloud, especially in those that have been lately sicke.”*

- John Evelyn, writing at the close of the seventeenth century tells us: '*Sprigs of Borage are of known virtue to revive the hypochondriac and cheer the hard student.*'
- Parkinson commends it '*to expel pensiveness and melanchollie.*'
- Bacon says that it '*hath an excellent spirit to repress the fuliginous vapour of dusky melancholie.*'
- Culpepper finds the plant useful in "*putrid and pestilential fever, the venom of serpents, jaundice, consumption, sore throat, and rheumatism*'
(cited in Grieve, 1931).

- In 1629 the great herbalist John Parkinson (1567-1650), apothecary to James I, mentioned: “*Borage and Bugloffe are held to bee both temperate herbes, being used both in the pot and in drinkes that are cordiall, especially the flowers, which of Gentlewomen are candid for comfits*” (Parkinson, 1904, p.252).

- The use of borage leaves to flavour cordials has a long tradition in Britain. Conserves and candied borage were also common preparations (Sinclair-Rohde, 1969).
- The Physiomedicalist herbal tradition in the United States adopted this European herb. The famed physician William Cook MD noted: *“Like other relaxants and demulcents, it acts fairly on the kidneys and bladder, and thus increases urination and relieves cystitis, and is of service in recent cystic and vaginal catarrhs. At one time it enjoyed a reputation in rheumatism, probably because of its diaphoretic and diuretic action. The infusion may be used freely; the fluid extract is given in doses of 10 to 30 drops three or four times a day”* (Cook, 1896, p.14).

Borage in Modern Research

- Borage may be a useful herb in the prevention of cancer due to its high phenolic content ([Lozano-Baena, et al., 2016](#)).
- An extract of Borage silver nanoparticles (AgNPs) has been found to have antibacterial and anticancer properties ([Singh et al., 2017](#)).
- A randomised controlled trial determined that Borage improved the clinical findings of asthma ([Mirsadraee et al., 2016](#)).
- There is a lack of systematic research for Borage exposing a gap in the literature for further research.



Symphytum officinale L.

- The famed historian Herodotus (c. 484–c. 425 BCE) recorded the use of the root for severe bleeding and bronchial ailments over 200 years ago (Flower & Marincola, 2002).
- In *De Materia Medica*, written in the first century, Dioscorides (c. 40-90 CE) described how *Symphytum* roots were used for internal haemorrhage: *“The roots below are black on the outside and white and slimy on the inside. Finely ground and then drunk they are beneficial for those spitting blood and those suffering from internal abscesses”* (Beck, 2011, p.257).
- In his *Naturalis Historia* Pliny the Elder (23-79 CE) mentioned a root decoction of comfrey taken with wine for kidney disease, intestinal cramping and bleeding of the lung (Bostock & Riley, 1856). Chapter 148 claims that comfrey ensures rapid healing of wounds and, in chapter 161, comfrey is mentioned as an emmenagogue when ground into dark wine.

- Greek physicians of the 7th century also used *Symphytum* in similar ways, establishing continuity of use. Comfrey is mentioned by Paulus of Aegineta (625-690 CE) in a formula for the spitting of blood, dosed at two spoonfuls; and also for intestinal ulcers and haemorrhage, for which Comfrey root was macerated in wine with Tragacanth (Adams, 1844).
- Centuries later the physician John Gerard (1545-1612) who was held in high esteem by the Royal Court of Elizabeth I noted: *“The slimie substance of the roote made in a posset of ale, and given to drinke against the paine in the backe, gotten by any violent motion, as wrestling, or over much use of women, doth in fower or five daies perfectly cure the same, although the involuntarie flowing of the seed in men be gotten thereby”* (Gerard, 1597).

- In the late 19th century in the United States a group of medical doctors called the Eclectics, who used herbal medicines extensively in response to what they considered the damage caused by allopathic medicine, left a century's worth of publications that continue to inform the herbal tradition to this day (Haller, 1994).
- It is worth noting that Eclectic Philosophy was underpinned by the concepts of *specific diagnosis* and *specific medicine*. In their medical philosophy the expressions of both disease and health were considered uniform (specific), and scrutiny of these expressions provided for the “rational practice of medicine” (Scudder, 1873/1994).

- In their particularly studied approach the Eclectics found no issues with *Symphytum*. Dr Finley Ellingwood (1852-1920), one of the major figures in Eclectic medicine, prescribed Comfrey internally for all forms of bronchial irritation or breathing difficulties, and for inflammation of the stomach and bowels.
- He also recounted a fellow MD who used the herb for over 30 years in his practice, employing a strong decoction of one ounce of root to a pint of water taken freely, and being especially useful in pneumonia (Ellingwood & Lloyd, 1919).

- In Russia, Comfrey is known as *knit-together herb* and has been used since Tsarist times as a poultice for bullet and shrapnel wounds. It has a much older use in Russian folk tradition, being mentioned in most Russian herbals for reducing pain in the intestinal tract. An internal remedy was also employed for bronchitis and tuberculosis. A standard decoction was 15g root in 250ml cold water brought to the boil; simmered for 15 minutes; cooled and dosed at 125ml three times daily (Zevin, 1997).
- Researchers who have studiously documented the use of plants in folk medicine in Britain and Ireland, list uses of Comfrey for external injuries in common with the ancients as well as for rheumatism, but also describe internal use for kidney disorders and for ridding the lungs of phlegm (Allen & Hatfield, 2004).

Comfrey in Modern Research

- There are several systematic reviews of clinical trials and literature reviews of comfrey ([Staiger, 2013](#); [Cameron & Chrubasik, 2013](#); [Gagnier et al., 2016](#)) extolling its virtues as an external remedy.
- One study considered practitioner use among practitioner associations: 75% (n=239) only reported on external use ([Frost, O'Meara & McPhearson, 2014](#)).
- There is a lack of systematic research for Comfrey exposing a gap in the literature for further research.

Concluding Remarks

- The 3 herbs considered have long term traditional use spanning 2000 years or more. There appears to be no accounts of contraindications for internal use within the ancient WHM tradition.
- A handful of methodologically-flawed case reports from the late 1980s onwards expressed some concern for PAs, which have not been borne out in practitioner experience. This can create tension between Allopathic and Herbal communities. Further research is needed.
- There is a need to reconsider the current hierarchy of evidence and challenge the dominance of the current reading of Evidence-Based Medicine (EBM).
- Current recommendations for the use of these 3 herbs still remain appropriate, though vigilance is continually necessary.

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