The study of herbal constituents has been part of the herbalist's repertoire for a long time – as "chemistry" since 1661, and as alchemy for long before that. The world of modern phytochemistry may seem intimidating or unnecessarily abstract, but it can also be a rich source of information that can guide our work as practitioners and medicine-makers. We can look at constituents in a variety of ways: focusing on their sensory or *organoleptic* qualities, considering their contributions to the energetic natures of the herbs in which they're found, and exploring questions of solubility & compatibility in remedies. By getting to know our herbs from this perspective – while always recognizing the variability, synergy, and individuality inherent in herbal medicines – we can become better herbalists.

phytochemistry on the macro scale

Year after year, study after study, the evidence mounts up: humans just plain *need* to be involved with lots of plants in lots of ways, and if you can't get your plant time by going out into the forest, you can get it by drinking a lot of tea.

constituents from the plant's point of view

Plants make two broad classes of constituents. First are the primary metabolites, which are necessary to sustain the life of the plant. These include proteins (including enzymes), lipids (fats), carbohydrates of various types – all serving functions analogous to those they perform in the human body – as well as chlorophyll, which is necessary for photosynthesis.

Then there are the secondary metabolites which, while not strictly necessary to sustain life, perform a variety of functions within the plant which increase its survivability and adaptability to changing situations. This is where the interesting phytochemical constituents of our herbs come into play.

We might wonder, why is it these plant chemicals are so active in animals and humans? It comes down to common ancestry. On the small scale, all the various chemicals plants produce are derived from the original product of photosynthesis, glucose – which is known in mammals as blood sugar. The structure of chlorophyll itself is extremely similar to hemoglobin, only with a magnesium atom in place of the iron – one more indicator of the similarities between people and plants. On the large scale, there's the common ancestry of humans and plants, as well as our long history of co-evolution. Basically, these compounds are active in both plants and people because, when you get right down to it, we're not really that different.

Indeed, the role these constituents play in plants is usually analogous to the role they play in the human body. It's often instructive to ask, what does this constituent do from the plant's point of view, and how does that compare to its effects in humans? Carotenoids, for example, protect the plant from oxidative damage due to excessive exposure to UV light, and can convey this protection to us if we eat a lot of them. Tannins fend off microbial infections in a plant's leaves and roots, and we can use them in a first aid application to prevent infection in a wound. Alkaloids, including caffeine, both fight microbes and discourage herbivores from eating a plant; in humans, though, their effects can be much more varied. It's not always a one-to-one correlation.

forest bathing

Another part of “being involved with lots of plants in lots of ways” requires us to consider the effects of "forest bathing", the act of going out into natural environments and deriving health benefits therefrom. This practice has been found to reduce the physiological effects of stress, improve immune function, lower blood pressure, and much more.

A variety of contibuting factors seem to be at play, including the mere sight of natural colors and shapes – the field of varied greens and browns, the absence of hard straight human-shaped edges – but in particular, the variety of aromatic compounds you're exposed to in a wild environment. Plants are communicating constantly through scents, and when we breathe them in, our bodies respond. (Richard Mandelbaum framed exposure to this panoply of wild aromatics as a "macrobiome" in this presentation.)

There’s no replacement for real forest time. Still, if we acknowledge the presence of various potent aromatic constituents in our herbs, and then learn how to make a good cup of tea, we can derive many of the same benefits even while we’re city-bound.

whoever eats the most vegetables wins

We inherited this slogan from Paul Bergner. It’s both a simple reminder that cuts across all forms of dietary dogma, as well as a summation of a variety of insightful observations about the relationship between varied and rich phytochemical intake and healthy outcomes. This helps us to step back a bit, from a limited focus on some specific constituent that has its fifteen minutes of fame (here’s looking at you, curcumin), to see the more general effects plant intake has. A favorite paper on this subject:

> The Metabolic Plant Feedback Hypothesis: How Plant Secondary Metabolites Nonspecifically Impact Human Health
> Jurg Gertsch, *Planta Med* 2016; 82(11/12): 920-929.

There are a few interesting points in this article, starting with the main one that low-potency phytochemicals like chlorophyll are more important to human health (specifically when it comes to metabolic and inflammatory illnesses) than the high-potency ones which make herbs medicinal – whoever eats the most vegetables wins again, see?

The author also argues that medicinal plant use was actually fairly infrequent among hunter-gatherer groups; that they had little call for it since they were ingesting high amounts of non-starchy plants: "It is tempting to postulate that the lack of bulk phytochemicals once ingested in pre-agriculturist times gradually had to be compensated by spices and herbal remedies in the carbohydrate farming societies to diminish the mismatch of ancient genes and new diets."

We might then compare that insight with something like these studies on the health of English people in the Mid-Victorian era, where again, high intake of fresh and wild greens led to surprisingly robust health. This boon was rapidly compromised in the following decades, however, with greater influx of sugar and refined grains, tinned meats, and condensed milk. Processed food, even moreso than early agriculturalists' starchy diets, is extremely deficient in phytochemistry.

In addition, most of our domesticated vegetables have lost a great deal of their nutrient content, due to generations of selective breeding for larger, sweeter varieties. This led to the loss of phytochemicals with bitter or strong flavors, which may please the palate but deprives the body of an ancestral protection.

Fortunately, herbs can provide part of the solution to this problem! Take a look at these values (from Pedersen's *Nutritional Herbology*) for basic mineral content for various herbs:

per 100 g (3.5 oz)	**calcium**	**iron**	**magnesium**	**chromium**
nettle *(Urtica dioica)*	2900 mg	4.2 mg	860 mg	390 mcg
burdock *(Arctium lappa)*	733 mg	14.7 mg	537 mg	200 mcg
peppermint *(Mentha piperita)*	1620 mg	6.0 mg	661 mg	trace
horsetail *(Equisetum arvense)*	1890 mg	12.3 mg	437 mg	220 mcg
comfrey *(Symphytum off.)*	1800 mg	1.2 mg	70 mg	180 mcg
kelp *(Fucus vesiculosis)*	3040 mg	1.6 mg	867 mg	70 mcg
ODI (optimum daily intake)	800 – 1200 mg	10 – 20 mg	400 – 800 mg	200 – 600 mcg

Three and a half ounces is a lot of herb, but remember, this is in the context of your entire diet. A quart of herbal tea a day, made with an ounce of these or other herbs blended together, can make up for a lot of deficiencies even in a processed-food-heavy diet. It's especially good at filling in the gaps created by modern agricultural methods, which tend to reduce the amount of micronutrients available in vegetables – even organic ones.

constituent energetics

Beyond basic nutrients, herbs carry rich and interesting phytochemistry.

These constituents can make gross adjustments or fine adjustments – compare the effects of chlorophyll versus those of caffeine, canadine, or capsaicin. Fine adjustment phytochemistry is one of those things that's thoroughly unreliable until you get your senses directly involved in your decision-making. This drives us necessarily towards *organoleptic* assessment – the use of your senses as a portable chemistry lab, to make determinations about an herb's actions, or the potency of an extract – as well as the broader category of what herbalists call "energetics".

There's a big starburst of trails to follow there, one interesting tail of which you can catch with an article like this one, where syndrome differentials from Traditional Chinese Medicine are used to improve clinical efficacy. That's a simple example of a trend we've observed – Chinese, Korean, Saudi, Iranian, Russian, and a multitude of other university nationalities have published studies including differentiation based on syndromes according to traditional medicine practices – whether from TCM, Unani, Ayurveda, or others – and in every case we've seen, they've found better results than those observed with conventional diagnostics. This is very clearly the most effective study design for assessing herbal therapeutic efficacies. It makes us wonder: when will we see these kinds of studies in the US? Or at least, acknowledged by the FDA and similar authorities?

visual organoleptics: color

Some constituents of herbs are detectable by looking at the color of the plant (or of an extract you make from it), because they reflect or absorb certain wavelengths of light. When you see these colors, here are some constituents you may expect to find:

red – **xanthophylls** (red-orange; oxygenated carotenoids, a type of terpene structure; antioxidant; examples include lutein, capsanthin, astaxanthin). some **anthocyanins**.

orange – **carotenoids** (yellow-orange; hide under green, may be present in green leafy vegetables; antioxidant, anticancer). curcumin (a polyphenol). **xanthophylls**.

yellow – **carotenoids**. curcumin.

green – **chlorophyll** (darker green = more), **folic acid** (name from 'foliage').

blue – **anthocyanins** (red-blue-purple; flavonoids, a type of polyphenol; antioxidant, anticancer, antiiflammatory).

purple – **anthocyanins**.

invisible – **OPCs** (astringent; antioxidant, anticancer, antiinflammatory, etc), some **flavonoids**.

olfactory & gustatory organoleptics: smell & taste

The smell and taste of an herb, as well as its texture or "mouthfeel" and other qualities often referred to as "impression", tell us a lot about an herb's activity. Scent and taste are our oldest senses, seated in the depths of the limbic brain – an ability to make chemical distinctions which is shared with not only other animals but also plants and microbes.

This is a skill worth developing! It takes time and practice. Taste an herb a day.

Whenever learning or working with a new plant (once you're positive it's safely identified), go through an organized process of organoleptic assessment. After looking at the color of the plant for any clues there, take its scent. Inhale deeply and repeatedly; it helps to exhale warm moist air on the plant between inhalations. Crush, break, rip, or otherwise disturb the integrity of your plant matter, then smell again. Now taste the herb, feeling for its quality and texture, chewing but not swallowing, for a couple of minutes.

In most herbs, the taste is a complex – for example, a plant like calamus *(Acorus calamus)*, which is pungent, aromatic, and bitter. This reflects the presence of several different types of constituents, which will act synergistically. Some constituents have distinctive tastes, like the capsaicin in cayenne *(Capsicum annuum)*, menthol in peppermint *(Mentha x piperita)*, or berberine in barberry *(Berberis vulgaris)* and others.

salty – Indicates the presence of **minerals**, and therefore, nutritive potential. Mineral salts occurring in plants are always more than mere sodium chloride (NaCl, table salt) – a variety of different minerals will be represented. Seaweeds are

the most obviously salty herbs, but horsetail, nettle, and many mineral-rich nutritive herbs also have some saltiness.

sweet – Primarily from various types of **carbohydrates**: simple sugars (mono- & disaccharides), as well as oligosaccharides (like inulin and FOS), and polysaccharides (starches, mucilagens, mucopolysaccharides). May also come from various **glycosides** (constituents bound to sugar molecules) – most famously the diterpene-based stevioside in *Stevia*, and the triterpenoid saponin glycyrrhizin found in licorice *(Glycyrrhiza glabra)*. The extraction menstruum glycerin is also sweet, comprised as it is of glycerol, a sugar alcohol. Sweet herbs are nourishing, moistening, and restorative.

mucilaginous – Long-chain **polysaccharides** provide the demulcent, moistening effects of mucilaginous herbs. These include mucilage itself, as well as pectins, gums, and mucopolysaccharides. (See **Appendix B: Demulcents** for more data on the mucilagen content of various herbs.) Honey, glycerin, and syrup preparations all add demulcency to the finished product.

aromatic – Plants with aromatic scent & flavor are generally dispersive, carminative, diaphoretic, diuretic, and upward-moving. These scentastes are conveyed by the volatile constituents, those which readily evaporate. In plants they often serve as chemical messengers. These are primarily the lighter terpenes – **monoterpenes** like menthol in mint *(Mentha)* and nepetalactone from catnip *(Nepeta cataria)*, and **sesquiterpenes** such as chamazulene in chamomile *(Matricaria recutita)* or zingiberene from ginger *(Zingiber officinale)*. Some polyphenols called **phenylpropanoids** are also volatile, e.g. eugenol from clove *(Syzygium aromaticum*, formerly *Eugenia aromatica)*, anethole from fennel *(Foeniculum vulgare)*, and apiole from parsley *(Petroselenium crispum*, formerly *Apium petroselenium)*.

diffusive – The tingly, "herbal pop-rocks" sensation you feel when you take a dropperful of good quality tinctures of *Echinacea*, spilanthes *(Acmella oleracea)*, or prickly ash *(Zanthoxylum clava-herculis)* is due to the presence of **alkamides**, lipid-based constituents that are fairly rare. Diffusive herbs stimulate circulation from the center to the periphery, and from the depths up to the surface.

pungent/spicy – The flavors indicative of carminative, stimulant herbs come from a variety of sources. Some terpenes are pungent as well as aromatic; the **resins** – compounds of heavier terpenes – produce the deepest flavor of their group. The amino acid derivatives known as **glucosinolates**, found in Brassicaceae (mustard family) plants, are strongly pungent; humans metabolize them into isothiocyanates like sulforaphane, which has shown some anti-cancer effects in trials – yet another reason to eat your greens! But perhaps the most potent pungent constituents are the **phenylpropanoid derivatives**: curcuminoids from turmeric *(Curcuma longa)*, gingerols & shogaols from ginger, capsaicin from cayenne – these bear real fire! Piperine from black pepper *(Piper nigrum)* is sometimes included in a group with those, too, but it can also be categorized as a **piperidine** alkaloid. Alkamides may also have pungency in their flavor profile.

bitter – All bitters are draining to stagnant fluids, and stimulate digestive secretions. Some of the most intensely bitter compounds known to humanity are the **secoiridoid monoterpenes**: gentiopicroside and amarogentin, found in *Gentiana* and relatives, are famous for this. Some **diterpenes** are bitter as well,

like the kahweol and cafestol found in coffee *(Coffea arabica)*. Outside the terpenes, select **flavonoids** taste bitter, like quercitin, and naringin. The ability to detect bitterness seems to be, in part, a method for identifying potentially poisonous plants; some of the most poisonous compounds in nature are from the category of alkaloids, and indeed, some of these are quite bitter. There are many subcategories (and sub-sub-categories) of alkaloids, but particularly worth exploring are the proto**berberines**; several of this group are potently antimicrobial.

sour – Sour herbs are cooling in effect. When it comes to sour flavor, it is the **organic acids**, a subgroup of carbohydrates, that do most of the work. Ascorbic acid (vitamin C), acetic acid (which comprises about 5% of apple cider vinegar), and citric, malic, and oxalic acids are all found in sour herbs like wood sorrel *(Oxalis acetosella)* and hibiscus *(Hibiscus sabdariffa)*. Occasionally some of the shorter **hydrolysable tannins**, part of the flavonoid polyphenols group, will have a sour taste too.

astringent – Sourness and astringency are closely related. All the **tannins** will have an astringent taste. As they get longer, developing into oligomeric proanthocyanidins (OPCs) and condensed tannins, they become more astringent and less sour. Likewise, plant **acids** will exert some astringent effect in their own right. Astringents tone & tighten lax tissues, and can help with wound healing.

There are a few other flavors you may encounter, like acrid – we specifically use this for the "vomit at the back of your throat" feeling – which in *Lobelia inflata* is in part attributable to the strongly relaxant piperidine alkaloid, lobeline. Some other flavors are less indicative of medicinal effect, like the meaty, savory, umami flavor generally indicating high protein content; or the nutty flavor of fixed oils.

taxonomic energetics

We try to always remain attentive to the energetic qualities of herbs – whether they are heating or cooling, moistening or drying, tonifying or relaxant to the human organism or its tissues. Because herbs are congregations of so many different constituents, this is a more useful way of describing their effects than it would be to, for instance, call st john's wort a serotonin reuptake inhibitor, or willow a COX inhibitor. Their actions are broader and deeper than those specific molecular effects, and are not analogous to the pharmeceutical actions of drugs isolated for those purposes.

The question arises whether individual constituents, or groups of them, could be described in this way also. Does this model transfer, or does it break down? As a first pass, we might come up with something like this:

heating – [aromatic, pungent, spicy.] alkamides. amines, cysteine sulfoxides, glucosinolates. phenylpropanoids, phenylpropane derivatives, anthraquinones. some terpenes. some alkaloids.

cooling – [bitter, sour.] mucilagens. cyanogenic glycosides. phenolic acids, stilbenoids, bioflavonoids. some terpenes. some alkaloids.

moistening – [sweet, demulcent; oily.] mucilage & related heteropolysaccharides. lipids.

drying – [aromatic, bitter, sour, astringent.] amines. volatiles. various phenolics & terpenoids. some alkaloids.

tonifying – [astringent.] acids. catechins, OPCs, tannins. some alkaloids.

relaxant – [acrid.] mucilagens. kavalactones. some alkaloids.

In my reckoning, this doesn't turn out to be a particularly useful analysis – certainly no more so than analysis based on tastes. In fact, it could be said that taste categories are ontologically prior to constituent categories, when it comes to energetic qualifications.

See **appendix A: Taxonomy**, and note that some categories there, which look minor or low-level, are in fact very important to us (e.g. tannins).

So: constituents can be detected and distinguished by their color, scent, flavor, and to some extent by their action on the body. Patterns start to emerge, we can discover principles governing their behavior.

constituent behaviors

Here we'll consider some ways in which various physical properties of constituents will influence their activity in medicines.

The practicalities here have primarily to do with medicine-making: identifying quality plant material, avoiding incompatible chemical mixtures, getting the constituents to the tissue we want to affect, and so on.

molecular weight

This is pretty simple: some molecules are larger than others: proteins, enzymes, polysaccharides, and complex tannins are the biggest. The larger they are, the heavier they are. This has implications for certain medicinal preparations, most especially the essential oils, but it's also relevant to steams, smokes, incense, and smudges.

Essential oils, or volatile oils, are made up of the lightest constituents in a plant: mono-, sesqui-, and diterpenes, as well as some lighter phenolics. Distillation separates these from the heavier constituents; they're present in plants in very small amounts, so each ½ ounce bottle of essential oil represents large amounts of harvested plant matter.

Only these volatiles are active in medicinal steam or smoke – so don't expect to get any demulcent effects from a marshmallow root steam! That might seem obvious, but sometimes it's not as apparent at first glance. Robert Tisserand has a nice article in which he uses these considerations to debunk the herban legend that frankincense essential oil, taken by the undiluted drop in the mouth, can stimulate immunity and cure cancer. As he explains, the primary anti-tumor compound boswellic acid has a molecular weight of 450 – 500, whereas all volatlie compounds have molecular weights below 300, so there is no boswellic acid in frankincense essential oil at all! (It's pretty much always a bad idea to take essential oils undiluted internally.)

solubility

The solubility of constituents in a given menstruum is influenced by their polarity, molecular size, and other structural characteristics, as well as the polarity, pH, and temperature of the menstruum itself.

Polarity is a somewhat complicated topic, but for our purposes here we can start by noting that water is the most polar menstruum we use for herbal extracts, and oils are the least polar. Polarity isn't an all-or-nothing binary state – constituents and media can be semi-polar to varying degrees. Glycerin, alcohol, and vinegar are on the polar side, while hexane (a chemical solvent sometimes used in commercial extracts) is very non-polar. The basic principle here is that *like dissolves like*: polar media extract polar constituents, and non-polar media extract non-polar constituents: this is the major factor that differentiates water-soluble constituents from oil-soluble ones.

> water-soluble constituents – carbohydrates in general, oligosaccharides (in hot water), mucilagens (in cold water), glycosides of all types (the sugar portion increases overall polarity), phospholipids, amines, phenolics, tannins, aromatics (especially in hot water/steam), saponins, some alkaloids.
>
> alcohol-soluble constituents – glycosides, phenolics, flavonoids, saponins, alkaloids.
>
> fat-soluble consituents – all lipids, cysteine sulfoxides, phenylpropanoid derivatives, triterpenoids, carotenoids, saponins, resins, steroids, steroidal alkaloids.

Polarity also accounts for the medicine-making guides to use a particular percentage of alcohol for your tinctures: greater alcohol concentrations will be less polar, and so may enable your tincture to pull out constituents that water alone would leave behind.

> low-alcohol tinctures (20 – 30%) – mucilagens, tannins, flavonoids, glycosides.
>
> medium-alcohol tinctures (40 – 60%) – essential oils, alkaloids, flavonoids, some glycosides, most saponins.
>
> high-alcohol tinctures (75 – 95%) – essential oils, resins, oleoresins.

The *pH* (acidity) of the menstruum is also a strong influence on constituent solubility, expanding the range of chemicals that will be pulled out into a water extraction. In this case the guideline is that *high pH menstrua extract low-pH constituents*, and vice versa. Alkaloids and amines will become much more water-soluble in acidic solutions – this is why we usually add 5 – 10% vinegar to tinctures of alkaloid-rich herbs like lobelia. On the other hand, some constituent groups like the flavonoids and organic acids will be more water-soluble in alkaline solutions.

compatibility

Some constituents don't play nice together.

If you mix tannins with alkaloids, proteins, or polysaccharides, they'll bind each other and fall out of solution, forming a precipitate. (From Michael Moore comes this

straightforwardly-named Bad Formula Combinations fact sheet, showing herbs high in tannins and those high in alkaloids.)

You can observe this for yourself! If you squirt a dropperful of high-alcohol (low-polarity) tincture of a resinous herb like myrrh or propolis into a glass of (highly polar) water, you'll see a cloud of particulates take shape. Likewise, if you pour some marshmallow root cold water infusion into a glass of high-proof alcohol, ropy strings of precipitated polysaccharides will coalesce into a ball of "snot" and sink to the bottom. Charming!

This can make it difficult to combine certain herbs or herbal extracts – even if they're both technically tinctures, they might be incompatible due to different polarities or constituent interactions. Sometimes this can be overcome – for example, adding a small percentage of glycerin to your formula (5 – 10%) may help prevent the precipitation of tannins when tinctures are made or blended.

variability

Herbalists recognize that not all parts of a given plant are equivalent when it comes to medicine – that dandelion *(Taraxacum off.)* root is more of a liver stimulant than the leaf, which is a stronger diuretic; or that only the rhizome of solomon's seal *(Polygonatum biflorum)* is medicinal, not its aerial parts. So constituent variability by part of plant should be simple to understand. There are some elements that do seem to consistently show up in certain plant parts; almost all berries, for instance, contain some plant acids.

There is substantial constituent consistency within (and variability between) plant families. For instance, all of the buttercup family (Ranunculaceae) plants produce the compound *ranunculin*, which is converted to an irritant toxin called *protoanemonin* when the leaves are bruised or broken. (This is why these plants aren't used fresh or eaten raw! The toxin breaks down to an inert substance with drying or cooking.)

Each species in the family will have a characteristic concentration of this substance, and each individual plant will also produce less or more based on soil and weather conditions, insect and microbe activity, and so on. Remember, the plants make these for their own purposes, and many times as part of defensive mechanisms. This is one reason why wild specimens, exposed to various stressors in less-than-ideal conditions, are frequently more potent than pampered cultivated plants – what doesn't kill them makes them stronger medicine!

Seasonal variation in constituent presence can be quite profound, and can have bearing on optimal harvesting practices. Many herbalists know that burdock *(Arctium lappa)* root is best harvested in the autumn of its first year, when the root is "fully charged" with a summer's worth of photosynthesized & stored energy – which largely takes the form of inulin, a prebiotic polysaccharide. If harvested too late in the plant's second year of life, it will have already used up these stores and the root will be less medicinal.

Those factors (and others) impact variation between and within plants – but there are also variations in individual human responses to different herbs. From a traditional medicine perspective, we look first at the impacts of *constitutional type* on a person's response to an herb or formula: giving hot and dry herbs to a hot and dry person, for instance, is likely to make their problem worse rather than better! This is the most important factor when it comes to individual variation, because it is really the sum total of a number of contributing elements – baseline metabolism, fluid dynamics, habitual tension patterns, and so on.

One place individual variation is being actively researched today is with investigations into the differences in microbiome composition between individuals. This does turn out to have direct bearing on herbal metabolism! In this study, it was shown that a person's habitual diet style (even just on the superficial level of "Western" vs "Asian") led to differences in their gut flora; since those gut flora play a big role in the metabolism of ginseng compounds, they influence how the body receives and reacts to ginseng use. Very likely, this sort of dynamic is at play for many interesting phytochemicals, especially the larger and more complex molecules.

synergy

The soul is greater than the hum of its parts. In the context of the full complex of constituents naturally occurring in a single plant, each one's effect may be altered from what it would be if the chemical were consumed solo. Some constituents' activities are amplified, others are smoothed out; some which seem inert when tested on their own will display important activities that would otherwise be missed.

Unfortunately, this phenomenon is difficult and costly to study, so although it's been an intuited principle of herbal medicine for as long as it's been practiced, scientific proof has been difficult to come by. This is changing in recent years, and there are some areas in particular where synergies have been demonstrated – most notably when it comes to antimicrobial activity against multi-drug-resistant bacteria and fungi.

There are many forms of synergy in herbal medicine – primarily to do with potentiation, attenuation, and stabilization.

Importantly, synergistic effects within a single herb may serve to increase the concentration of a particular chemical at its active site[s] in the body. That is, one "complementary" compound may improve the stability, solubility, or active life of an "active" constituent. This appreciation of plant complexity, which becomes intuitively obvious to everyone who works intimately with plant medicines, is borne out in practice by the long litany of purported "active constituents" which have been found to be less effective in isolated form than when taken in minimally-processed or "crude" extracts.

Vitamin C, for instance, is better absorbed when consumed in citrus fruits, with all their bioflavonoid complexity, than in the form of pure ascorbic acid. Full-spectrum extracts of st john's wort *(Hypericum perforatum)*, which include the plant's procyanidins, show better antidepressant effects than isolated hypericin. In some cases isolation and concentration can even be dangerous, as when the rush for high-kavalactone extracts led some manufacturers to use the stems and leaves instead of the roots, and led to some cases of liver toxicity.

Sometimes synergies between different herbs in formulation have to do with metabolism and *bioavailability* – a measure of how much of the constituent is actually absorbed or utilized by the body. The addition of saponin-rich herbs to a formula can increase the solubility of other, less water-soluble compounds. This accounts for some of the capacity of licorice *(Glycyrrhiza glabra)* to act as a "harmonizer" in formulae, helping potentially incompatible herbs to "play nice" together.

researching constituents

When researching the qualities and activities of a constituent, or when hearing about them second- or third-hand, it's easy to get seduced by the apparent certainty conveyed by the trappings of science. We have to guard ourselves against a number of common mistakes.

misconceptions

- **fallacy #1: "the" "active" constituent** – This is the common idea that an herb's effects are reducible to the activity of one particular stand-out chemical. As we've seen, synergy among multiple constituents of an herb is often much more important to its overall effect than is any single molecule it produces. And indeed, much of the efficacy of herbs has to do with how the body *reacts* to these constituents than to their direct chemical action – think of how bitter constituents can have a rapid and profound reflex effect on the entire gastrointestinal tract, which is not dependent on those constituents circulating to the organs themselves.

- **fallacy #2: herbs as weak drugs** – Arising out of #1 comes the idea that herbs "work" the same way as drugs do, by targeting a specific molecular process in the body, but are simply weaker than pharmaceuticals because they are "dilute" or "dirty". Instead, we need to keep sight of the idea that herbs operate in distributed, multifactorial ways on multiple levels: from basic mineral content, to high-concentration/low-activity chemicals like chlorophyll, to the more active and exciting phytochemistry of terpenes, alkaloids, and so on. This will never be reducible to a single drug-like action, and in most cases, *this is a strength.*

- **fallacy #3: "in" is as good as "on"** – One considerable advantage (thought it does come with numerous drawbacks) which pharmaceuticals have over herbs is their convenience factor: an antibiotic pill can be given by mouth and yet still have effects on distant organs or tissues in the body. Herbs, by and large, don't work this way: you have to *get the herb to the tissue*. Antimicrobial herbs taken orally will generally exhaust their effects in the gastrointestinal tract; some famously antimicrobial constituents like berberine will not even be absorbed through the intestinal mucosa. If you want to disinfect the sinuses, you need a steam or neti pot; if you want to resolve cellulitis, you need a soak or some other topical application. So, when reading about "antibiotic" herbs in particular, make sure to consider whether the constituents (or a relevant reflex action they initiate) can actually reach the tissue you're trying to affect.

This is by no means an exhaustive list of pitfalls! These are the most common, though, by far. Taking steps to monitor for and root them out of your own thought processes is an important application of critical thinking when doing herbal or phytochemical research.

desirable details

To the extent possible, we want to acquire the following information about our constituents of interest.

- **name[s]** – That might seem obvious! But it's worth checking to see if your constituent goes by more than one name. The PubChem Compound database is a good place to check. Names also might tell you something about your chemical – for instance, if its name ends in *-ine*, it's probably an alkaloid (e.g. caffeine, berberine, lobeline).

- **taxonomy** – What chemical groups or families does your constituent belong to? If you find it difficult to narrow this down, don't despair! Phytochemical taxonomy, it turns out, is not particularly well standardized. Many constituents belong to more than one category, or don't fit neatly into any standard categories. Think of this only as a way to identify potentially useful information, not as a progress-blocking necessity.

- **forms occurring in plants** – Chemicals often occur in multiple forms within or across plants – generally due to a base compound forming a complex with another functional group. For instance, salicylic acid occurs as methyl salicylate, salicin, salicortin, and other variants in different herbs. A very general case here is that of *glycosides* versus *aglycones* – sugar-bonded compounds versus those that have had their sugars cleaved off (e.g. rutin, one of several possible glycosides of quercetin, the aglycone). Sometimes these various forms behave quite differently from each other: methyl salicylate is volatile, but salicin is too heavy to evaporate; all glycosides are very polar and so very water-soluble, but their aglycones may not be.

- We may also be interested in **related pharmaceutical compounds** used as drugs.

- **physical properties** – For all forms of interest, including molecular weight, pH (or rather, solubility in acid/alkaline menstrua), and polarity.

- **purposes in plants** – For comparison, and for potential insights into activity in humans or other animals.

- **plants of notable content** – How much do they really have? How much constitutes a relevant dose? We'll also try to get a sense for how various doses of the herb (or herbal preparation) comprise doses of the constituent. It's great to know "there's X chemical in Y herb", but you also need to know if it's present at physiologically relevant levels. A good rule of thumb here: if a constituent is present as 1% by weight of the herb, then one gram of herbal material will provide 10 milligrams of that constituent.

- **pharmacokinetics & pharmacodynamics** – These somewhat intimidating terms refer to the ways in which the chemical moves through and affects the body. They have much to do with the various transformations performed by digestive fluids, microbial metabolism, and liver/kidney/gut "detox" processes. The circulation and excretion of these constituents are also of interest. Sometimes this has therapeutic relevance: the sulfur compounds in garlic are directed toward the lungs to be eliminated, giving you garlic breath but also conveying their antimicrobial effects to the lung mucosa as they pass through them on the way out. This happens even if you originally absorbed them through your skin, like in a foot bath!

- **documented effects** – Including whenever possible a note on the **level of evidence** for those effects: theoretical, *in vitro*, animal studies, human trials. In many instances, a good case study series is much more compelling than a petri dish experiment!

- **"side effects" / undesirable effects, contraindications, cautions** – Always look for these! We're also on the watch for undesirable **interactions**, whether those are with other constituents, herbs, drugs, foods, or anything else the person might also be ingesting.

- **synergies** – Which might be considered as "positive" / beneficial interactions, both within the set of constituents found within a plant, as well as potential synergies with constituents from other herbs in a formula. These may readily impact all of the prior considerations.

A number of other quantifications may also be of interest when considering the effects of a constituent. If possible, we would like to know:

- **minimum effective dose** (MED) – Dose below which the substance is ineffective.

- **maximum tolerated dose** (MTD) – Dose above which the substance produces undesirable effects.

- **therapeutic window** – The difference between the MID and the MTD. If this is small, or if the MTD is less than the MED, the substance has limited utility or is a poison.

- **median effective dose** (ED_{50}) – The dose required to achieve a medicinal effect in 50% of test subjects. (Note that this will be a different number for different effects of the same constituent: e.g. lobeline at low doses is a bronchodilator, at high doses it's an emetic.)

- **toxic dose** (TD_{50}) and **lethal dose** (LD_{50}) – Doses at which toxic or lethal effects occur.

- **minimum inhibitory concentration** (MIC) – For antimicrobial substances, the concentration at which the substance inhibits microbial activity/growth. Compare with **sub-inhibitory concentration** (SIC), as well as **minimum bactericidal concentration** (MBC).

See **Appendix C** for an example constituent monograph.

Don't despair if you can't find or figure out all of these numbers. They will neither make nor break your remedy's efficacy!

When in doubt, always return to what you can see, smell, taste, and feel. Trust your senses, and don't discount what you observe just because something written in sciencese says it couldn't happen.

Don't let the diagrams scare you! Don't let the long names drive you away. Phytochemistry can be intimidating at a first look, but it does have some useful insights to offer even the most folksy of healers. The best parts of it are those that bear directly on your practical experience working with herbs.

For everything from honing our senses, recognizing variability, appreciating synergy, providing clues to underutilized therapeutic applications, and aiding in medicine-making and formulation decisions, it turns out that phytochemistry can actually be pretty practical, after all!

Ryn Midura
May 2017

carbohydrates	monosaccharides	glucose fructose arabinose xylose galactose mannose rhamnose
	disaccharides	sucrose maltose lactose
	oligosaccharides	inulins fructooligosaccharides FOS
	polysaccharides	homopolysaccharides starch cellulose mucilagens mucilage gums pectins immunomodulators ^{2}-glucans arabinogalactans acemannan mucopolysaccharides (glycosaminoglycans – GAGs) agar carrageenans alginates fucoidan
	organic acids derived from monosaccharides	fruit acids citric malic tartaric oxalic acetic formic ascorbic

lipids	fatty acids	saturated SFA	stearic myristic lauric palmitic arachidic caprylic ➢ ±-lipoic acid
		unsaturated UFA	monounsaturated oleic É-9 palmitoleic É-7
			polyunsaturated linoleic (LA) É-6 alpha-linolenic (ALA) É-3 gamma-linolenic (GLA) É-6 docosohexaenoic (DHA) É-3 eicosapentaenoic (EPA) É-3
		trans TFA	conjugated linoleic (CLA) UFA ➢ TFA via: hydrogenation oxidation heating
	oils	triglycerides (triacylglycerols)	
	waxes		
	alkamides	alkylamides alkenylamides alkynylamides	\ isobutylamides /
	polyalkynes (polyacetylenes) ➢ thiophenes	*Echinacea pallida/ simulata* polyalkyne ketones falcarinol, falcarindiol panaxydol, panaxynol, panaxydiol, panaxytriol arctinal PHT	
	polyalkenes (polyenes)	*Echinacea pallida/ simulata* polyalkene ketones	
	phospholipids	lecithin phosphatidylcholine phosphatidylserine	

amino acids & derivatives	**amino acids**	**standard** – 22 total; plant/animal protein-forming **other** – hundreds, varied functions ornithine betaine L-theanine 5-hydroxytryptophan (5-HTP)
	amines	histamine ephedrine synephrine **methylxanthines** caffeine theobromine theophylline cathinone mescaline
	cysteine sulfoxides	alliin + alliinase ➢ allicin allicin + time ➢ sulfides, ajoene, vinyldithiins
	gamma-glutamylcysteines	S-allylcysteine S-*trans*-1-propenylcysteine S-allylmercaptocysteine
	glucosinolates (thioglucosides) ➢ isothiocyanates diindolylmethane (DIM) sulforaphane	glucobrassicin glucoraphanin
	cyanogenic glycosides ➢ thiocyanates	prunasin amygdalin sambunigrin
	enzymes	

phenolic compounds	simple phenols	arbutin ➢ hydroquinone
	phenolic acids	gallic gentisic ellagic salicylic vanillin
	phenylpropanoids	chlorogenic acid caffeic acid rosmarinic acid rosavins volatile / oil-soluble: eugenol anethole apiole ^{2}-asarone eugenol cinnamaldehyde safrole estragole
	coumarins	esculetin scopoletin umbelliferone fungi ➢ dicoumarol furanocoumarins
	lignans	silymarin schisandrins gomisins secoisolariciresinol matairesinol podophyllotoxin
	phenylpropane derivatives	curcuminoids gingerols shogaols capsaicinoids
	stilbenoids	resveratrol
	xanthones	norathyriol gentisein mangostin
	styrylpyrones	kavalactones kavain methysticin yangonin

phenolic compounds		
	flavonoids	chalcones isoliquiritigenin xanthohumol
		flavanols catechin, ... epigallocatechin gallate (EGCG), etc theaflavins, thearubigins
		proanthocyanidins oligomeric ~ (OPCs) condensed tannins
		hydrolyzable tannins gallotannins quercitannins ellagitannins
		anthocyani[di]ns cyanidin pelargonidin malvidin peonidin
		flavonols quercetin rutin hyperoside kaempferol myricetin
		flavones luteolin apigenin
		flavanones naringin / naringenin hesperetin / hesperidin eriodictyol / eriodyctin
	isoflavones (isoflavonoids)	genistein daidzein glycitein formononetin biochanin A
	benzofurans	usnic acid
	chromones	khellin

phenolic compounds	quinones	benzoquinones ubiquinone / CoQ_{10} vitamin K
		naphthoquinones juglone lawsone plumbagin
		anthraquinones emodin barbaloin rhein chrysophanol cascarosides sennosides
		naphthodianthrones (bianthraquinones) hypericin pseudohypericin
	phenolic ketones (phloroglucinol derivatives)	hyperforin adhyperforin cannabinoids tetrahydracannabinol (THC) cannabinol cannabidiol humulone lupulone

terpenes	monoterpenes	volatiles linalool limonene menthol pulegone thymol cineole thujone nepetalactone pinene iridoids aucubin catalpol valepotriates secoiridoids gentiopicroside amarogentin swertiamarin / sweroside
	sesquiterpenes	volatiles ±-bisabolol chamazulene zingiberene petasin valeranone valerinic acid lactones artemisinin absinthin taraxacin achillin parthenolide matricin helenin lactucin, lactupicrin
	diterpenes	phytol carnosol grindelic acid stevioside rebaudioside dulcoside ginkgolides marrubiin andrographolide forskolin cafestol, kahweol paclitaxel grayanotoxin
	triterpenes	cimifugoside actein
	triterpenoid saponins	eleutherosides glycyrrhizin gymnemic acids aescin ursolic acid oleanolic acid

terpenes	tetraterpenes (carotenoids)	lycopene carotenes (± / ² / ³ / ´) xanthophylls (oxygenated carotenoids) lutein neoxanthin violaxanthin capsanthin, capsorubin astaxanthin

steroids	steroidal saponins	ginsenosides dammaranes protopanaxadiol protopanaxatriol pseudoginsenosides oleanols diosgenin
	phytosterols	beta-sitosterol campesterol stigmasterol
	cardiac glycosides	convallatoxin digitoxin, gitoxin, gitaloxin

alkaloids	betalain	betacyanins	betanidin isobetanidin betanin
		betaxanthins	indicaxanthin vulgaxanthin
	diterpenoid	aconitine, aconine, etc condelphine, delphinine, etc	
	imidazole	pilocarpine	
	indole	ergoline	ergine, ergotamine, etc lysergic acid
		monoterpenoid	gelsemine, gelsedine, etc ibogaine, ibogamine, etc reserpine, deserpidine, etc strychnine, brucine vinblastine, vincristine yohimbine
		quinoline	quinine, quinidine cinchonine, cinchonidine
		beta-carboline	eleagnine harmine, harmaline, etc
		simple indoles	gramine psilocin, psilocybin
	isoquinoline	tetrahydro-isoquinolines	anhalamine anhalonine pellotine lophophorine
		benzyltetrahydro-isoquinolines	papaverine tubocurarine aporphines aristolochic acid boldine protoberberines berberine canadine hydrastine palmatine jatrorrhizine coptisine tetrahydropalmatine sanguinarine etc chelidonine etc protopine pavines
		morphinans	morphine codeine

alkaloids	isoquinoline	phenethyl-isoquinolines	colchicine
		monoterpenoid isoquinolines	cephaeline psychotrine emetine
	piperidine	lobeline, lobelanine, lobelanidine piperine coniine, conhydrine, etc pelletierine, etc	
	pyridine	nicotine arecoline	
	pyrrole	tetrapyrrole	**chlorophyll***
	pyrrolidine	hygrine, cuscohygrine	
	pyrrolizidine	saturated	tussilagine nemorensine, parsonine, etc
		unsaturated	simple crotanecine heliotridine etc monoesters intermedine indicine etc diesters uplandicine symphytine etc macrocyclic senkirkine jacobine senecionine petasitenine etc
	quinolizidine	lupanine, lupinine, anagyrine sparteine, ammodendrine	
	steroidal	solanidine / solanine, solasodine / solasonine tomatidine / tomatine jervaine, veratramine, etc	
	tropane	hyoscyamine, scopolamine atropine cocaine	

*** Chlorophyll** is a *chlorin ring* (a cyclic tetrapyrrole / a heterocyclic *aromatic* [cyclic, planar, stable] ring of 3 pyrroles + 1 pyrroline) holding a central magnesium ion, with one or more side chains (usually phytol, a diterpene). It is not usually considered an alkaloid *per se*, but it shares structural qualities and derivations with them.

Information derived primarily from *Herbal Constituents* by Lisa Ganora (1st ed, 2009).

How much mucilage does it take to be notably/usefully demulcent?

It turns out that mucilage *per se* is not the only constituent that contributes to demulcency.

PLANT	BOTANICAL NAME	PART	MUCILAGE	OTHER MUCILAGENS
marshsmallow	*Althaea off.*	root	5.0 – 35.0%	pectin 11.0 – 35.0%
				polysaccharides 25.0 – 35.0%
		leaf	6.0 – 15.7%	
		plant	to 21.0%	arabinogalactan *
slippery elm	*Ulmus rubra*	bark	4.1 – 35.0%	pentosans 12.0 – 18.0%
comfrey	*Symphytyum off.*	root	to 29.0%	gum 5.0 – 10.0%
coltsfoot	*Tussilago farfara*	leaf	to 8.2%	(tannin to 17.0%)
		flower	to 6.9%	(inulin *)
borage	*Borago off.*	plant	11.0 – 30.0%	(tannin to 3.0%)
hibiscus	*Hibiscus sabdariffa*	calyx	1.5 – 65.0%	pectin to 3.2%
pomegranate	*Punica granatum*	pericarp	0.6 – 24.0%	pectin 2.0 – 4.0%
				gums to 3.2%
fenugreek	*Trigonella foenum-graecum*	seed	18.0 – 50.0%	(fixed oil 10.3 – 20.0%)
okra	*Abelmoschus esculentus*	fruit	to 0.6%	seed: pectin to 2.2%
linden	*Tilia spp.*	flower	* (Chevallier 3%)	
licorice root	*Glycyrrhiza glabra*			pectin 1.4 – 9.0%
aloe vera	*Aloe vera*	leaf	*	acemannan *
				glucomannan *
		plant	*	(mucopolysaccharides *)
prickly pear	*Opuntia ficus-indica*	stem	*	pectin *

PLANT	BOTANICAL NAME	PART	MUCILAGE	OTHER 'MUCILAGENS'
cinnamon	*Cinnamomum verum*	bark	2.0 - 3.7%	
	C. aromaticum/cassia	bark	*	
violet	*Viola tricolor*	plant	to 9.5%	
dandelion	*Taraxacum off.*	root	1.1 – 8.5%	pectins 1.7 – 12.0% (inulin 4.3 – 30.0%)
evening primrose	*Oenothera biennis*	plant	*	(tannin to 11.0%)
plantain	*Plantago major*	plant	*	(tannin 4.0 – 5.7%)
		seed	7.5 – 25.0%	gum 3.0 – 10.0%
	P. psyllium	seed	6.5 – 40.0%	
	P. ovata	seed	10.0 – 30.0%	arabinoxylans 17.0 – 25.5%
flax	*Linum usitatissimum*	seed	2.0 – 8.4%	pectin 5.4 – 10.0%
chia	*Salvia hispanica*	seed	* (src 5.0–6.0%)	
mullein	*Verbascum thapsus*	flower	*	
		seed	to 0.4%	
calendula	*Calendula off.*	flower	to 1.5%	
chickweed	*Stellaria media*	plant	1.7 – 20.0%	
blessed thistle	*Cnicus benedictus*	plant	1.6 – 20.0%	(Chevallier: lignans, tannins)
bladderwrack	*Fucus vesiculosus*	plant	*	algin[ates] 4.1 – 50.0% fucoidan to 60.0%

Values derived from Duke unless (otherwise noted). * *Listed but unquantified.*

Many demulcent plants were not listed in the database, e.g. dulse *(Palmaria palmata)*, Irish moss *(Chondrus crispus)*, Iceland moss *(Cetraria islandica)*, & solomon's seal *(Polygonatum biflorum)*.

salicylates

- **constituent name** – salicylic acid

- **taxonomy** – phenolics > polyphenols > phenolic acids

- **forms in plants** – some free salicylic acid will be found. more often, the compounds:
  - *methyl salicylate* – a volatile methanol ester
  - *salicin* – a glucoside
  - *salicortin* – a glycoside

- **related pharmaceutical compounds**
  - *acetylsalicylic acid*, aka aspirin
    - antipyretic, antiplatelet/antithrombotic, COX-inhibiting antiinflammatory/analgesic.
    - the acetyl group is what provides the blood-thinning effects; since this is not present in plant-sourced froms of SA, they do not thin the blood.
    - aspirin is metabolized in the upper GI to salicylic acid, which is why it can irritate the gut lining and cause ulcerations. plant-sourced salicylates will not do this.

- **physical properties**
  - *molecular weight*
    - salicylic acid – 138
    - methyl salicylate – 152
    - salicin – 286
    - salicortin – 424
  - *polarity* – all forms are polar, especially the glycosides.

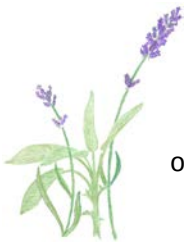
- **purposes in plants**
  - *hormone & pheremone* – released in response to predation or infection, signals other leaves and nearby plants to release more deterrent / antimicrobial compounds, recruits beneficial insects to fend off the attackers.
  - *antimicrobial* – prevents proliferation of detrimental bacteria and fungi.

- **plants of notable content**
  - willow *(Salix alba)* – bark 0.4 – 11% salicin, average 1%.
  - poplar, cottonwood *(Populus spp.)*
  - alder *(Alnus spp.)*
  - wintergreen *(Gaultheria procumbens)* – leaf 0.5 – 0.8% methyl salicylate.
  - birch *(Betula lenta)* – bark 0.2 – 0.6% methyl salicylate.
  - meadowsweet *(Filipendula ulmaria)* – essential oil to 1.5% methyl salicylate.

- **organoleptic qualities**
  - *color* – none.
  - *scent* – methyl salicylate has the distinctive “wintergreen” scent.
  - *taste* – astringent, bitter, “cool” flavor.

- **energetic qualities** – cooling, drying (draining), tonifying.

- **pharmacokinetics**
  - salicin – after ingestion, metabolized in upper GI to salicyl alcohol, then in intestines/liver to salicylic acid. only about a third of ingested salicin will be metabolized to salicylic acid.



- salicylic acid is ultimately be excreted in the urine, therefore useful for the pain and inflammation caused by urinary tract infections.

- **pharmacodynamics** – nonselective COX inhibition: blocks prostaglandin release, antiinflammatory.

- **effects & applications** – like all phenolic acids, antioxidant and antiinflammatory. documented as analgesic, antiinflammatory, antioxidant, antipyretic, antirheumatic, antitumor, fungicidal (MIC 1000 ug/ml), hypoglycemic.

- **dosage**
  - we find effective doses of willow tincture in the range of 1 – 8 ml of 1:4 tincture (equivalent to ¼ g – 2 g of powder, 2.5 – 20 mg salicin).
  - German Commission E considers willow bark effective for headache, rheumatic pain, fever at doses of 6 – 12 g powder = 60 – 120 mg salicin.
  - compare with "usual adult dose" of aspirin for pain/fever, 325 – 650 mg.
  - upper tolerable dose depends on sensitivity to astringency.

- **contraindications & cautions**
  - *incompatible* with cold, dry, tense constitutional type or tissue states.
  - *toxic* to cats and dogs.

- **undesirable interactions**
  - often found in tannin-rich herbs, which will lead to precipitation if mixed with alkaloids, proteins, polysaccharides.

- **known synergies** – some complementary constituents found in willow:
  - *apigenin* – anti-inflammatory, antispasmodic
  - *quercetin* – anti-inflammatory, antiallergenic/antihistaminic
  - *catechins* – antioxidant, anti-inflammatory, anticancer, antidiabetic, "anti-aging", cardioprotective
  - *tannins* – astringent, bacteriostatic, vulnerary