Solubility of Herbal Constituents

Relative polarity of the common solvents used in herbal extraction:

Water 1.00
Glycerol (glycerin) 0.812
Ethanol (EtOH) 0.654

Mixing water and ethanol together (hydroethanolic), in different proportions, determines the overall polarity of the solvent mixture. The higher the water percentage and the lower the ethanol, the higher the overall polarity (since water is more polar than ethanol). Conversely, the lower the water percentage and the higher the ethanol, the lower the overall polarity will be (since ethanol is less polar than water). So a 24 % EtOH tincture would have 76 % water and would be very polar, while a 95 % EtOH tincture would have only 5 % water and would be much less polar.

For detailed solubility of individual, isolated molecules, consult the Merck Index (Merck & Co., Inc., Whitehouse Station, NJ).

Solubility in a given solvent is influenced by the polarity of a molecule's skeleton and functional groups, the molecular size, temperature, the pH of the solution, and other factors. The solubility of an isolated compound is easy to determine, but this may change in the complex matrix of a medicinal plant extract. The general principle: **like dissolves like**. A high-polarity solvent will pull high-polarity molecules out of the herbal material; a low-polarity solvent will select for low-polarity molecules.

Carbohydrates

- Monosaccharides (e.g., glucose, fructose): highly water soluble
- Organic acids (e.g., citric acid, formic acid; generally water soluble, varies with pH)
- Disaccharides (e.g., sucrose, maltose: highly water-soluble)
- Oligosaccharides (e.g., inulin, FOS: water-soluble, esp. in hot water)
- Heteropolysaccharides (e.g., mucilages, gums: highly water-soluble)
- Homopolysaccharides: starch: hot-water soluble; cellulose: insoluble
- Dietary fiber: soluble (includes heteropolysaccharides such as mucilages, gums, and pectins) and insoluble (e.g., cellulose, lignin)
- Carbohydrates generally stay dissolved in low-ethanol (~ 20 – 30%) preparations and in glycerites
- Carbohydrates generally will precipitate out at higher ethanol ratios
- Tannins can bind to and precipitate complex carbohydrates

Lipids

- Fatty acids (e.g., Omega 3s, EFAs, PUFAs, DHA, EPA): mostly oil-soluble; slight solubility in ethanol
- Triglycerides (= triacylglycerols: oils like Olive or Almond, also known as 'fixed oils,' are mostly composed of triglycerides): very slightly soluble in ethanol, not in water; will dissolve many oil-soluble compounds
- Phospholipids (e.g., lecithin, phosphatidyl choline, PS) are emulsifiers
- Waxes (e.g., beeswax): soluble in warm oils but not in cold
- Alkamides (e.g., the tingly isobutylamides in *Echinacea* & *Spilanthes*): soluble in mid-concentration ethanol (around 40 – 60 %)

- Polyacetylenes (e.g., arctinal from Burdock; PHT from *Bidens*) similar to alkamides
- Unsaponifiable matter (anything dissolved in an oil, such as Olive, which is not a fatty acid or triglyceride; includes oil-soluble vitamins, phytosterols, carotenoids, etc.)
- Essential oils are not lipids, but rather are composed mainly of small terpene compounds; soluble in mid-to-high percentage ethanol, fixed oils, slightly soluble in water
- Lipids generally soluble in other lipids

Amino acids & derivatives

- Free amino acids at pH ~ 7 are zwitterions; very water-soluble; generally soluble in low-percentage EtOH
- Some sulfur-containing amino acid derivatives (e.g., ajoene and sulfides from Garlic) are oil-soluble; some sulfides have limited water solubility
- Cyanogenic glycosides (e.g., amygdalin, prunasin) soluble in water, more so in hot water, somewhat soluble in cold EtOH, more so in hot EtOH
- Amines: like alkaloids, generally more soluble in acidic media; amine salts water-soluble (ionic)
- Methylxanthines (e.g., caffeine): hot-water soluble, less so in cold water
- Peptides: (e.g., glutathione) generally water-soluble; depends on pH (lose solubility at the isoelectric point)
- Proteins: generally water-soluble; depends on pH (lose solubility at the isoelectric point)
- Enzymes: generally water-soluble; depends on pH (lose solubility at the isoelectric point)
- Proteins and enzymes denature in EtOH
- Tannins can bind and precipitate proteins

Phenolic compounds

Structures of phenolic compounds (polyphenols) vary widely, and many can occur as either glycosides or aglycones. Glycosides are generally more water-soluble than the aglycones. Depending on pH, the hydroxyl groups may be ionized; this enhances water-solubility.

- Phenolic acids (solubility varies with structure and pH)
- Phenylpropanoids (solubility varies with structure and pH)
- Coumarins (glycosides generally water- and ethanol-soluble; aglycones less so)
- Lignans (generally soluble in acetone/water; Flaxseed lignans are not oil-soluble)
- Phenylpropanoid derivatives (e.g., capsaicin, curcumin, gingerol: soluble in high-percentage ethanol, fixed oils)
- Stilbenoids (e.g., resveratrol; soluble in EtOH)
- Xanthones (generally soluble in EtOH and oils)
- Styrylpyrones (e.g., kavalactones; soluble in high-percentage EtOH, acetone)
- Flavonoids (solubility varies, but many are water and EtOH-soluble)
    - Anthocyanins: water- and EtOH-soluble
    - OPCs: water- and EtOH-soluble
    - Tannins: smaller tannins soluble in hot water, EtOH; larger tannins relatively insoluble
- Isoflavonoids: soluble in EtOH; low water-solubility; however, the glycosidic forms are more water-soluble
- Benzofurans: (e.g., usnic acid; soluble in hot EtOH; solubility in water and EtOH is very low)
- Chromones (e.g., khellin; soluble in hot water, hot EtOH)
- Quinones (e.g., anthraquinones; solubility varies; most soluble in water and EtOH; bianthraquinones in *Hypericum* are oil-soluble)

- Phloroglucinol derivatives (e.g., hyperforin, cannabinoids: soluble in oil and high-percentage EtOH)

Terpenoids (terpene compounds)

As a general rule, terpenoids tend to be oil- and high-percentage EtOH soluble. Triterpene and steroidal saponins are water-soluble because of their sugar groups. The smaller terpenoids (in essential oils) have very limited solubility in water, and are soluble in fixed oils and EtOH. Small terpenes include:

- Hemiterpenes
- Monoterpenes
- Sesquiterpenes

The larger terpenes are not volatile and tend to be oily or resinous substances. In general, they are soluble in fixed oils or high-percentage EtOH. Many resinous materials are composed of larger terpenes (and/or polyphenolic aglycones):

- Diterpenes
- Triterpenes
- Tetraterpenes (carotenoids)

The aglycones of triterpenoid saponins (sapogenins) are practically insoluble in water or EtOH, while their glycosidic forms are highly water-soluble and amphiphilic (soapy/foamy).

Steroids

Plant steroids are oil-soluble, with the exception of glycosidic forms (e.g., steroidal saponins and cardiac glycosides); the latter are slightly water-soluble.

- Phytosterols (soluble in fixed oils, high-percentage EtOH)
- Steroidal saponins (aglycones are not water-soluble, glycosidic forms are)
- Cardiac glycosides (slightly water-soluble; more so in dilute alcohol; aglycones oil-soluble)

Alkaloids

The pH of the solution influences the solubility of alkaloids. In general, alkaloids are more oil-soluble in high pH (alkaline) solutions. Conversely, they are more water-soluble in acidic solutions. Most alkaloids are soluble in mid- to high-percentage ethanol/water solutions.

Capsaicinoids (pseudo-alkaloids) are oil-soluble.

The purple and yellow betalain alkaloids (found in Beet, Pokeberries, Prickly Pear Cactus, Amaranth, etc.) are very soluble in water and will remain dissolved in low-to-mid ethanol solutions.

The isoquinoline alkaloids are soluble in moderate-to-high ethanol solutions with the exception of berberine, which is far more water-soluble than the others.

The N-oxide forms of pyrrolizidine alkaloids (PAs) are very water-soluble. PAs are soluble in low-pH solutions, but insoluble in high-PH solutions. They are also soluble in ethanol and in organic solvents such as acetone. They are nearly insoluble in fixed oils.

Polarity of solvent solutions

The overall polarity of a solvent mixture depends on the ratios of ethanol and water (and glycerin if you are using it) in it. Adding glycerine (glycerol) could either raise the overall polarity of an ethanol/water solvent mixture, or could lower it, depending on this ratio.
One way to measure the polarity of a compound is
to give it a number called the 'dielectric constant':

Water 80
Glycerol 46
Ethanol 25

You can determine the polarity of a solvent mixture by multiplying the volume fraction of each solvent times its dielectric constant and summing.

For example,

If you are using 50% ethanol and 50% water, without any glycerol, your overall polarity would be 52.5:
(.50)(25) + (.50)(80) = 52.5

if you are using 50% Ethanol, 45% water, and 5% glycerol, your overall polarity would be (.50)(25) + (.45)(80) + (.05)(46) = 12.5 + 36 + 2.3 = 50.8. So in this case, replacing 5% of the *water* with glycerol would decrease the overall polarity of the mixture.

What if you replaced 5% of the *ethanol*, rather than 5% of the water, with glycerol? The overall polarity would be 53.55. So in this case you have increased the polarity of the mixture (relative to just ethanol + water).

Websites with table of relative polarities, densities, etc. for organic solvents:
http://www.iqo.csic.es/pagperso/afm/disolven.htm#TABLE%202 and
http://www.speckanalytical.co.uk/products/Tips/bps.html.

This page has a good not-too-technical explanation of how polarity works:
http://palimpsest.stanford.edu/byauth/burke/solpar/solpar4.html It's from this paper on solvent theory: http://palimpsest.stanford.edu/byauth/burke/solpar/

Average Ethanol Percentages for Fluid Extracts & Tinctures

Commonly used Ethanol Percentages for Fluid Extracts & Tinctures		
Low ethanol (20 – 40 %)	**Medium ethanol (40 – 60 %)**	**High ethanol (60 – 90 %)**
Cleavers ~ 30 – 35 %	Artemisia annua (Sweet Annie) ~ 50 – 55 %	Angelica ~ 70 – 75 %
Eleuthero (Siberian Ginseng) ~ 30 – 35 %	Astragalus ~ 40 – 45 %	Arnica ~ 65 – 70 %
Eyebright ~ 30 %	Black Walnut ~ 40 – 45 %	Ashwaganda ~ 60 – 65 %
Ginseng (Panax spp) ~ 20 – 30 %	Bladderwrack ~ 40 – 45 %	Black Cohosh ~ 80 – 85 %
Gotu Kola ~ 25 – 30 %	Bloodroot ~ 55 – 60 %	Buchu ~ 75 – 85 %
Green Tea ~ 25 – 30	Blue Vervain ~ 40 – 45 %	Cayenne ~ 80 – 85 %
Horsetail ~ 30 – 35	Boneset ~ 40 – 45 %	Chaparral ~ 70 – 75 %
		Chickweed ~ 65 – 70 %
Licorice ~ 20 – 25 %	Bugleweed ~ 50 – 60 %	Cinnamon ~ 65 – 70 %
		Devil's Claw ~ 60 – 65 %
		Elecampane ~ 65 – 70 %
Marshmallow ~ 25 – 30 %	Burdock ~ 50 – 60 %	Fennel seed ~ 60 – 65
Pau D'arco ~ 25 – 30 %	California Poppy ~ 55 – 60 %	Ginger ~ 70 – 80 %
Red Root ~ 30 – 40 %	Cat's Claw ~ 60 – 65 %	Goldenseal ~ 60 – 65 %
Reishi ~ 20 – 25 %	Celandine ~ 50 %	Grindelia ~ 65 – 70 %
Willow bark ~ 15 – 20 %	Chamomile ~ 50 – 60 %	Holy Basil ~ 65 – 75 %
	Cilantro ~ 50 – 60 %	Jamaican Dogwood ~ 70 – 80 %
	Coptis ~ 50 – 60 %	Kava Kava ~ 80 – 90 %
	Cornsilk ~ 50 – 55 %	
	Cramp Bark ~ 50 – 55 %	Lavender ~ 80 – 85 %
	Damiana ~ 55 – 60 %	Milk Thistle ~ 65 – 75 %
	Dandelion ~ 40 – 45 %	Myrrh ~ 85 – 90 %
	Devil's Club ~ 50 – 55 %	
	Echinacea ~ 45 – 50 %	Olive Leaf ~ 85 – 95 %
	Fo-Ti ~ 40 – 45 %	Oregano ~ 65 – 75 %
	Ginkgo ~ 55 – 60 %	Osha ~ 70 – 75 %
	Goldenrod ~ 50 – 55 %	Passionflower ~ 65 – 75 %
	Hawthorn ~ 40 – 45 %	Peppermint ~ 80 – 90 %
	Helonias ~ 40 – 45 %	Propolis ~ 80 – 90 %
	Hyssop ~ 50 – 55 %	Raspberry ~ 60 – 65
	Lemon Balm ~ 45 – 50 %	Rosemary ~ 65 – 70 %
	Lobelia ~ 40 – 45 %	Sage ~ 70 – 75 %
	Maca ~ 50 – 60 %	Saw Palmetto ~ 80 %
	Mistletoe ~ 45 – 50 %	Thyme ~ 70 – 75 %
	Motherwort ~ 55 – 60 %	Turmeric ~ 60 – 70 %
	Muira Puama ~ 55 – 60 %	Usnea ~ 90 – 95 %
	Mullein ~ 40 – 45 %	Vitex ~ 70 – 75 %
	Nettle ~ 50 – 55 %	Wormwood ~ 70 – 75 %
	Oat ~ 45 – 50 %	Yerba Mansa ~ 70 – 75 %
	Oregon Grape ~ 40 – 50 %	Yerba Santa ~ 70 – 75 %

Low ethanol (20 – 40 %)	**Medium ethanol (40 – 60 %)**	**High ethanol (60 – 90 %)**
	Plantain ~ 50 %	Yohimbe ~ 70 – 75 %
	Pleurisy Root ~ 40 – 45 %	
	Red Clover ~ 40 – 45 %	
	Rhodiola ~ 40 – 60 %	
	St. Johnswort ~ 50 – 60 %	
	Sarsaparilla ~ 40 – 50 %	
	Schizandra ~ 55 – 65 %	
	Shepherd's Purse ~ 40 – 45 %	
	Stillingia ~ 50 – 55 %	
	Stoneroot ~ 45 – 50 %	
	Uva Ursi ~ 50 – 60 %	
	Valerian ~ 50 – 60 %	
	Wild Geranium ~ 50 – 55 %	
	Wild Yam ~ 55 – 60 %	
	Wood Betony ~ 55 – 60 %	
	Yarrow ~ 55 – 60 %	
	Yellow Dock ~ 40 – 45 %	

Metric and Common Units of Measurement			
Mass (≈ weight)	**Closest Common Unit**	**Conversions**	**Conversions**
micrograms (mcg or µg)	very small unit; no common equivalent	1,000 mcg = 1 mg	1,000,000 mcg = 1 gram
milligrams (mg)	small unit; no common equivalent	1,000 mg = 1 g	
grams	ounces (dry weight, not fluid ounce) – an ounce is roughly 30 grams	1 gram = 0.0353 ounces [a teaspoon of table sugar weighs ~ 5 grams]	1 ounce = 28.35 grams
kilograms (kg)	Pounds	1 kilogram = 2.205 pounds	1 pound = 0.454 kilograms
Volume			
microliters (mcL or µL)	very small unit; no common equivalent	1,000 µL = 1 mL	1,000,000 µL = 1 liter
milliliters (mL)	fluid ounces (fl oz) – a one-ounce tincture bottle holds ~ 30 mL	1,000 mL = 1 liter a tincture-bottle eyedropper delivers ~ 1 mL	1 fluid ounce (fl oz) = 29.57 mL 1 milliliter = 0.0338 fl oz
liters (L)	Quarts	1 liter = 1.057 quarts	1 quart = 0.946 liters or 946 mL
Temperature			
Fahrenheit (F)	water boils: 212 °F water freezes: 32 °F ethanol boils: 173.3 °F	to convert F to C: multiply temp in F by 0.556, then subtract 17.8 room temperature: ~ 68 °F body temperature: ~ 98.6 °F	
Celsius (C)	water boils: 100 °C; water freezes: 0 °C ethanol boils: 78.5 °C	to convert C to F: multiply temp in C by 1.8, then add 32 room temperature: ~ 20 °C body temperature: 37 °C	