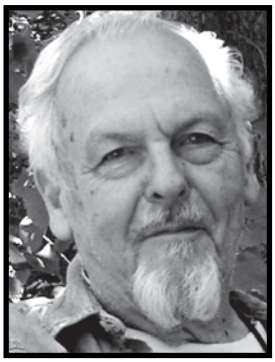
Herbal Superdrugs for the Superbugs!

James Duke, PhD



In his distinguished career, James Duke served the US Department of Agriculture for over 30 years. Before retiring, he developed his online ethnobotanical and phytochemical database. It is one of the most frequently consulted areas of the USDA website. Duke grows hundreds of plats on his six-acre Green Farmacy Garden with his wife, Peggy. Since retiring from the USDA, Dr. Duke served for five years as Senior Science Advisor to Nature's Herbs and with allherb.com. Since 2001, he has been a distinguished herbal lecturer at Tai Sophia Healing Institute (now Maryland University of Integrative Health). He has written over 30 books on medicinal plants.

Could cannabis be the superdrug of the year? In an effort to compile lists of herbs and phytochemicals that might help control some of the emerging superbugs, I was intrigued to find that five of the cannabinoids in *Cannabis sativa* were quite active against methicillin-resistant *Staphylococcus aureus*, commonly known as MRSA. Along with this important information about cannabinoids, I share in this rant a quick list of herbs and phytochemicals that have shown promise against MRSA and also methicillin-sensitive *Staphylococcus aureus* (MSSA), as well as some other species are also cited herein as "anti-*Staphylococcus*."

A particularly interesting paper compared the anti-*Staphylococcus* actions of the principal cannabinoids with pharmaceuticals. Under lead author Giovanni Appendino, the scientists studied four pharmaceuticals against a panel of six strains of *Staphylococcus* getting a wide spectrum of minimum inhibitory concentrations (MICs): erythromycin MIC=0.25->128 ug/mL; norflaxacin 0.5-128 ug/mL; oxacillin 0.25-128 ug/mL; and tetracycline 0.25-128 ug/mL. Keeping in mind that the lower the MIC, the more potent the chemical, that makes the cannabinoids look pretty good indeed, with low MICs: tetrahydrocannabinol (THC) 0.5-2 ug/mL; cannabidiol (CBD) 0.5-2 ug/mL; cannabinol (CBN) 1 ug/mL; cannabichromene (CBC) 1-2 ug/mL; and cannabigerol (CBG) 1-2 ug/mL (PubMed ID 18681481). I'm surprised no one has yet tried to encapsulate some of these in silver nanoparticles.

As this edition of the *JAHG* focuses on botanical essential oils, I'll point out that noted cannabis researcher Ethan Russo posed the question, "Are cannabis terpenoids relevant to the effects of cannabis?" in a paper entitled "Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects" (PubMed ID 21749363). Terpenoids are components of essential oils that give a plant (in this case cannabis) its distinctive scent. Over 200 terpenoids have been identified in cannabis, but Russo's paper singles out eight, all of which are widely distributed in the plant world and are GRAS (Generally Regarded as Safe) by FDA standards. They are listed here with examples of common plants that contain them:

Limonene, commonly found in lemons
Alpha-pinene, commonly found in pine
Beta-myrcene, commonly found in hops
Linalool, commonly found in lavender
Beta-caryophyllene, commonly found in black pepper
Caryophyllene oxide, commonly found in lemon balm
Nerolidol, commonly found in oranges
Phytol, commonly found in green tea

This study notes that while each terpenoid has its own set of pharmacological actions ranging from anti-inflammatory to

anxiolytic, they may also act synergistically with cannabinoids to treat various diseases as well as to counteract effects of THC. More to the point of this article, the aromatic component pinene, commonly found in pine as well as in cannabis, was found to be effective against MRSA. Combined with the powerful anti-MRSA actions of the cannabinoids mentioned above, cannabis as an anti-MRSA agent is looking better all the time.

Big Pharma, CDC and FDA once praised antibiotics, often monochemical derivatives of fungi, as the wave of the future. That failed future has come and gone! "Better living through (synthetic) chemistry" was an illusion generated by synthetic chemists, failing to appreciate that new synthetics can have many unanticipated side effects. Still today, monochemical superdrugs are failing. They say they have nothing new on track for the superbugs of the future. But there is still hope; the hope resides in our long-used herbs, those herbs the FDA has continuously and studiously tried to brainwash us into believing are useless. (Corporate crime I call it, rampant in America.)

Searching for the new "superdrug" (promising anti-MRSA herbs), I searched through the PubMed abstracts all the way back to 2010. Once again, as in many of my bacterial and viral compilations, Manuka honey seems very promising. I know no reason why Manuka should be better than our American honeys, especially if spiked with the more promising of the anti-MRSA herbs and phytochemicals listed below. Some synergies may make the combos "super," i.e. superlative to the monochemical antibiotics, slowly or rapidly yielding to drug resistance, which should have been anticipated.

Many of the PubMed abstracts give a relative idea of the potency of anti-MRSA herbal extracts and phytochemicals. I like in particular the MIC (minimum inhibitory concentration) usually but not always less than the MBC (minimum bactericidal concentration). Frequently they are compared with the MICs and MBCs of the many antibiotics, some lower, some higher. And I suppose (read: hope, but sometimes skeptically) most of these herbal and phytochemical studies are just as reliable as the PubMed pharmaceutical studies. Still I fear that some herbalists and phytochemists may be as aggressive and statistically manipulative at over-promoting their beliefs and products as Big Pharma scientists and reps. They may not even publish the negative points (or may completely leave negative studies unpublished). Too often, like too many Big Pharma scientists, they just publish the data that prove their point, and may sell their product. How I long for that utopian day when a benevolent FDA will support unbiased clinical comparisons of the natural herbal polychemical alternatives with the monochemical synthetics. My evolutionary homeostatic bias is that the herb will usually outperform the synthetic, when cost, efficacy and side effects are all considered.

Many authors compared their species with pharmaceuticals (including ampicillin, azithromycin, carbapenems, ceftazidime, chlorhexidine, ciprofloxacin, erythromycin, fluoroquinolones, gentamicin, levofloxacin, methicillin, norfloxacin, oxacillin, tetracycline, and vancomycin). Many authors also noted that the natural phytochemicals often potentiate the pharmaceuticals, often dramatically so. (A warning: my superficial compilation is often based only on the PubMed abstracts. In cases where there was a free publication, or the author sent PDFs, I dug deeper. In all cases where the authors did not cite the potency of their extracts or phytochemicals, I assume those extracts or phytochemicals were only modestly anti-MRSA.)

If we can believe the PubMed authors and the compiler (yours truly), the following are some natural phytochemicals which might individually be competitive or synergistically super-competitive with the failing pharmaceuticals with their reported MIC (in ug/mL).

But let me remind you as someone should have told BigPharma, using any one of these natural phytochemicals alone to fight a multi-drug resistant (MDR) ailment can rapidly lead to resistance, as in quinine long ago, and now artemisinin. Using quinine alone instead of the mix of more than a dozen alkaloids cohabiting with quinine was a BIG mistake. We are better off using many anti-MRSA natural chemicals in synergy to avoid this problem. I

Species	Common Name	Notes	PubMed ID(s)
Acorus calamus	Calamus		17440624, 17004300
Allium sativum	Garlic		17510266
Alpinia officinarum	Lesser galangal		18604497
Alstonia scholaris		AntiMRSA ethanol ext.	24749692
Armoracia rusticana	Horseradish		17260672
Asphodelus microcarpus		(emodin, (5)10-(chrysophanol-7'-yl)-	
		10-hydroxychrysophanol-9-anthrone, & Aestivin antiMRSA	24079182
Backhousia citriodora	Lemon ironwood		11893412
Caesalpinia sappan Linn.		AntiMRSA Caesanine-A, Caesanine B	24004304
Camellia sinensis	Tea		18781360, 23905026
Cinnamomum spp.	Cinnamon	EO AntiMRSA	19473851
Cipadessa cinerascens		Two weak MRSA chemicals	24915831
Citrus x limon	Lemon	EO AntiMRSA	19473851
Citrus x paradisi	Grapefruit	EO AntiMRSA	19473851
Combretum inflatum		4 MRSA IC45-14 =16 ug/mL; 3-7 reduced the growth of MRSA at 16 ug/mL	23978065
Curcuma longa	Turmeric		16161063
Cymbopogon spp.	Lemongrass	EO AntiMRSA	19473851, 23199627
Eucalyptus		EO AntiMRSA	19473851, 23199627
Kaempferia pandurata	"Temu kunci"	AntiMRSA MIC 16ppm AntiMSSA MIC=8 ppm	24783777
Kunzea sp	Kunzea	EO AntiMRSA	19473851
Laurus nobilis	Bay		18758079, 19783935
Lavandula angustifolia	English lavender	EO AntiMRSA	19473851, 16741725
Mangifera indica	Mango		17440624
Melaleuca spp.		EO AntiMRSA	19473851, 23199627
Mentha x piperita	Peppermint	EO AntiMRSA	19473851, 11549238
Mentha spicata	Spearmint		11549238
Mesua spp.		AntiMSSA, AntiMRSA	24089682
Morinda citrifolia	Noni		16883283
Nasturtium officinale	Watercress		17260672
Piper longum	Long Pepper		17145734
Piper nigrum	Black Pepper		17145734
Polyalthea longifolia		(16alpha-hydroxycleroda-3, 13 (14)z-dien-15,16-olide MIC 15.6-31.2 mg/l; (pretty weak, I'd say)	23989974
Psoralea corylifolia	Scurfy pea	Corylifolinin, neobavaisoflavone AntiMRSA	24199566
Punica granatum	Pomegranate		17566148
Rosmarinus officinalis	Rosemary		18556162
Salvia officinalis	Sage	EO AntiMRSA	19473851, 17541170
Santalum album	Sandalwood	EO AntiMRSA	19473851
Strobilanthes formosanus	Indigo	antiMRSA (poss. isatin and tryptanthrin)	24284490
Syzygium aromaticum	Clove	EO AntiMRSA	19473851, 17380552
Tabernaemontana alternifolia		AntiMRSA	24066905
Tagetes minuta L.		AntiMRSA	24689306
Tetradium rutaecarpum	Evodia	Quinolines MIC= 8-128 ug/mL; esp. evocarpine	24497124
Thymus spp.	White thyme	EO AntiMRSA	19473851
Tinospora cordifolia		AntiMRSA ethanol ext.	24749692
Thymus vulgaris	Thyme		19576738
Tropaeolum majus	Nasturtium		17260672
Zanthoxylum piperitum	Sichuan pepper		16794323

cannot imagine Big Pharma was not aware that using just one chemical, natural or synthetic, leads to resistance. The more chemicals, natural or synthetic, the less the probability of resistance. But why even bother to synthesize unnatural chemicals unknown to your genes. Your genes know the naturals (at least those consumed by your ancestors), not tomorrow's synthetics. Viva la natural synergies!

Furthermore, I suspect the whole herbs, like cannabis with its five anti-MRSA cannabinoids, or licorice, which contains dozens of antiseptic compounds, may synergistically be better anti-MRSA weapons than any one of the single compounds mentioned at left. And better yet, continued use of the mixtures will not likely lead to resistance like monochemical approaches will. On another hand, many species of *Hypericum* contain anti-MRSA activities and/or phytochemicals, but no single species so far is reported to contain a huge number of anti-MRSA phytochemicals. Thirty-three of 34 chloroform *Hypericum* extracts showed anti-MRSA activity, 5 with MIC=64 ug/ml. This genus has great potential for anti-MDR activity (PubMed ID 12234572). Many *Hypericum* species also contain hyperforin, one of the more potent anti-MRSA phytochemicals. Mangosteen (*Garcinia mangostana*) seems also to be well endowed with a variety of anti-MRSA phytochemicals.

Turning back the pages of time, let us look back to the safer herbs, many of which have 5,000-10,000 biologically active compounds in them, dozens or even hundreds of which are natural antiseptics. Many of the same natural phytochemicals can synergistically potentiate the failing pharmaceuticals. Unlike synthetics, these phytochemicals have been known to your genes for as long as your ancestors (primates or even earlier ancestors before) consumed them.

A sample of some of the more potent anti-MRSA phytochemicals and their MIC in ug/mL:

Achyrofuran	0.07
Ivesinol	0.31
Rubraxanthone	0.31-1.25
Tetrahydrocannabinol	0.5-2
Cannabidiol	0.5-2
Cannabinol	1
Hyperforin	1
Cannabigerol	1-2
Aphagrandinoid-A	1.57
Alpha-mangostin	1.95
Garciniacowone	2
23-methyl-6-o-desmethylauricepyrone	2
Silybin	2-8
Gamma-mangostin	3.13
Erybraedin-A	3.13-6.25
Eryzerin-C	3.13-6.25
Trigoflavidol-A & B	3.12-6.25
(z,z)-5-(trideca-4,7-dienyl)resorcinol	4
3,4-seco-mansumbinoic-acid	4
Erypostyrene	6.25
3′-(gamma,gamma-dimethylallyl)-kievitone	8
8′-(gamma,gamma-dimethylallyl)-wighteone	8