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Botanical Adulterants Program
BOTANICAL ADULTERANTS BULLETIN

on Adulteration of *Hypericum perforatum*

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Goal: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of St. John's wort (*Hypericum perforatum,* Hypericaceae) to the international herbal industry and extended natural products community in general. It is intended to complement the previously published works with information on St. John's wort (SJW) adulteration, e.g., the American Herbal Pharmacopoeia (AHP) SJW monograph,[1] by presenting new data on the occurrence of adulteration, the market situation, and consequences for the consumer and the industry.

St. John's Wort *Hypericum perforatum*
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1 General Information

1.1 Common name: St. John's wort

1.2 Other common names:

English: Common St. John's wort, perforate St. John's wort, goatweed, Klamath weed, racecourse weed, tipton weed[2-4]

Chinese: Guan ye lian qiao (贯叶连翘),[3-5] (千層樓)[2]

Dutch: Sint-janskruid[2,3]

French: Millepertuis, herbe à mille trous; millepertuis perforé, herbe de la Saint Jean, toutsaine[2,3]

German: Johanniskraut, Johannisblut, Herrgottsblut, Tüpfelhartheu, Tüpfel-Johanniskraut[2,3]

Italian: Iperico, erba di San Giovanni, iperico perforato, perforata, pilatro[2,3]

Portuguese: Hipericão, milfurada[3]

Russian: Zveroboj obyknovenny,[4] zwieroboij[2,3]

Spanish: Corazoncillo, hierba de San Juan, hipericón[2,3]

South African: Johanneskruid[3,4]

Swedish: Äkta johannesört,[4] Johannesört[3]

1.3 Accepted Latin binomial: *Hypericum perforatum* L.[6,7]

1.4 Synonym: *H. vulgare* Lam.[3]

1.5 Botanical family: Hypericaceae

1.6 Botanical taxonomy: The genus *Hypericum* consists of over 490 species, which are subdivided into 36 sections. SJW is a member of the section Hypericum, which also includes the closely related species *H. attenuatum*, *H. elegans*, *H. maculatum*, *H. scouleri*, *H. tetrapterum*, and *H. undulatum*, among others.[8-10] SJW shares many morphological features in common with *H. attenuatum* and *H. maculatum* in particular and it is thought that SJW arose from a hybrid cross between these two species. Identification is complicated by the fact that *H. perforatum* forms hybrid back-crosses with these species (see Robson[9] for a key to identify SJW hybrids). Natural populations of SJW are composed mostly of tetraploids but diploids, hexaploids and polyploids also occur. Based on morphological features and geographical ranges, Robson described four intergrading subspecies of SJW, subsp. *perforatum*, subsp. *chinense*, subsp. *songaricum*, and subsp. *veronense*.[9,10]

1.7 Distribution range: SJW is broadly distributed throughout the temperate regions of the world. Its natural range includes all of Europe (except the extreme north), northwest Africa, Canary Islands, Madeira, Azores, Turkey, Cyprus, the Levant (eastern Mediterranean countries) and western Saudi Arabia to northwest India (Uttar Pradesh), Transcaucasia, Turkmenistan to Altai, the Angara-Sayan region and northwestern Mongolia. In China, *H. perforatum* subsp. *songaricum* is limited to northwestern Xinjiang near the border with Kazakhstan and *H. perforatum* subsp. *chinense* is distributed throughout much of the country, from eastern Qinghai and Gansu, east to Hebei, south to Jiangxi and west to Yunnan.[8-10]

SJW has been introduced into many other parts of the world; it is a naturalized weed in Canada, United States, Mexico, Cuba, Haiti, Brazil, Uruguay, Argentina, Chile, Sudan, South Africa, Réunion, Australia, New Zealand, and Japan. In many of these countries, the proliferation of SJW has led to its classification as noxious weed that is subject to concerted efforts to eradicate it.[4,9-11]

1.8 Plant part, form, and production method: The dried flowering aerial parts, collected just before or during flowering, consisting of stem, leaves, buds, flowers, and fruit (capsules) are sold cut, powdered, and as aqueous infusions, oil infusions, and aqueous-alcohol extracts. Types of extracts include tinctures (1:5), fluid extracts (1:1), and powdered extracts. The extracts are often standardized to contain 0.3% hypericin or 2-5% hyperforin as markers for consistency.[1]

1.9 General use(s): As an herbal medicine, SJW is predominantly used for the treatment of mild-to-moderate depression. Other uses include anxiety, restlessness, insomnia, neuralgia, pain, and inflammation. As a dietary supplement, SJW is typically represented as "supporting emotional well-being" or other similar structure and function claims. Oil preparations are used internally to treat inflammatory gastrointestinal conditions, and topically to treat bites, bruises, burns, hemorrhoids, lacerations, muscle pain, sunburn, urticaria, and wounds.[1,12]

2 Market

2.1 Importance in the trade: From 2012 to 2015, retail sales of SJW dietary supplements in the Natural channel in the United States (US) remained relatively constant with only a slight decline/increase each year. Similar trends can be observed for sales in the Mainstream Multi-Outlet channel where sales and rankings from 2013 to 2015 have been quite consistent. The 2012 sales data, which are significantly higher in this channel, include numbers from Walmart, club, and dollar stores. Data from these retailers were no longer available in the following years.

In addition to the dietary supplement industry, SJW is used as an ingredient in the distillation of vodka, herbal tea, and as a source of red, yellow, purple and orange dyes.[3]

2.2 Market dynamics: For the dietary supplement market in the United States**,** SJW was a relatively obscure plant used in traditional medicine until the late 1990s when it skyrocketed in popularity following major media cover-

Table 1. SJW Dietary Supplement Sales in the US from 2012-2015

Channel	2012		2013		2014		2015	
	Rank	Sales [US$]	Rank	Sales [US$]	Rank	Sales [US$]	Rank	Sales [US$]
Natural[a]	32	2,310,361	34	2,265,796	36	2,289,098	35	2,461,235
Mainstream Multi-Outlet[b,c]	19	12,149,908	29	5,774,343	34	5,577,820	35	6,046,190

[a] According to SPINS (SPINS does not track sales from Whole Foods Market.)

[b] According to SPINS/IRI (The Mainstream Multi-Outlet channel was formerly known as the Food, Drug, and Mass Market channel [FDM], exclusive of possible sales at Walmart, a major retailer in the US and beyond.)

[c] Data for 2012 are according to Symphony/IRI and include Walmart, club stores (Sam's, Costco), military and dollar stores. Sources: T. Smith (American Botanical Council) e-mail to S. Gafner, September 2, 2015 and September 3, 2015. K. Kawa (SPINS) e-mail to S. Gafner, July 11, 2016.

age of European clinical research documenting its safety and efficacy for the treatment of mild-to-moderate depression. In 1998, SJW was the second best-selling botanical dietary supplement in the US mainstream market.[13] The soaring demand quickly out-paced the supply from wildcrafters in Europe and the United States, driving up the wholesale price and motivating manufacturers to secure new sources of supply. This global shortage in supply led to the appearance of commercial SJW products from Asia and in some cases, of unknown origin containing other species of *Hypericum* with differing chemical compositions and no proof of efficacy.[14,15] "Given the variation of the constituents, it was suggested that the drugs could not be considered as pharmaceutically and therapeutically equivalent" to the SJW extracts with clinically documented efficacy.[15]

The first reports of interactions between SJW and several classes of prescription drugs were published in 1999 and were rapidly followed by others in the years 2000-2003. These articles received considerable negative publicity and sales began to falter. In the Mainstream Multi-Outlet channel, SJW fell to fifth place in 2001 and sales continued to drop dramatically in 2002 (-40%), placing SJW in seventh place.[16,17] Over the following decade, US sales of SJW continued to decline, albeit more gradually (see Table 1 for 2012-2015 sales data). While it is tempting to blame the decrease in US sales of SJW on the safety concerns raised by herb-drug interaction studies and case reports, and questions raised about the touted anti-depressant benefits after a highly publicized large NIH-funded clinical trial had a negative outcome in people with major depression,[18] the glut of adulterated products with dubious therapeutic benefits which appear to have become more available in the market also may have contributed to the deterioration in SJW popularity in the US market.*

2.3 Supply sources: The supply of SJW for the European herbal medicine market was traditionally obtained from wildcrafters in Eastern European countries.[12,19,20] Some of the global supply still comes from these sources; according to the International Trade Centre (ITC) Market Insider (2015), European manufacturers obtain most of their raw material from producers and suppliers in Albania, Austria, Bosnia and Herzegovina, Bulgaria, Croatia, Germany, Hungary, Italy, Kosovo, Poland, Romania, Serbia, and Macedonia.[21]

In North America, SJW was traditionally harvested from naturalized plants in the Pacific Northwest and eastern states.[1] In 2015, most of the North American supply of commercial SJW extracts was obtained from China (R. Das [BI Nutraceuticals] e-mail communication, September 15, 2016).

3 Adulteration

Known adulterants: Other *Hypericum* species that have been identified as historical SJW adulterants include *H. barbatum*, *H. hirsutum*, *H. maculatum*, *H. montanum*, *H. tetrapterum*,[22] *H. patulum*,[23] and *H. crux-andreae* (syn. *Ascyrum crux-andreae*, *Ascyrum stans*).[24]

Also the following admixture of dyes have been reported as co-occurring SJW adulterants: E123 Amaranth (FD&C Red #2), E133 Brilliant Blue (FD&C Blue #1), E110 Sunset Yellow (FD&C Yellow #6), and E102 Tartrazine (FD&C Yellow #5).[25]

3.2 Sources of information confirming adulteration: Historically, scientific reports of SJW adulteration in the United States may be traced back to 1876.[24] Although there are no published systematic reviews on adulteration of SJW, there are numerous reports of adulteration in the literature based on morphological, chemical, and genetic evidence.

3.2.1 Morphological and chemical evidence: In the book *Teedrogen*, Wichtl (1984) stated that SJW is frequently adulterated with the *Hypericum* species *H. barbatum*, *H. maculatum*, and *H. montanum* which co-occur within the range of SJW.[26] Berghöfer and Hölzl (1986) also reported that SJW is frequently adulterated with other species of *Hypericum*, which occur within the European range of SJW, and added the species *H. hirsutum* and *H. tetrapterum* to this list.[22] They also remarked that SJW often interbreeds with the species *H. maculatum* and H. *tetrapterum* to form hybrids with intermediate features that are more challenging to classify taxonomically. Mitra and Kannan (2007) briefly mention that, in India, where the availability of SJW is limited, the Indo-Nepal species *H. patulum* is sold as *H. perforatum*.[23]

In 1998, Kurth and Spreeman observed that the boom in the US market and subsequent shortage of high quality material corresponded with the appearance of "more and more" poor quality products with chemical profiles that differed significantly from those of the clinically proven European SJW extracts.[14] They describe a proliferation of commercial extracts from the "Far East" (Asia) and "Chinese herb" with relatively high levels of quercetin (degradation product), significantly lower levels of other flavonoids, especially rutin, isoquercitrin, and biapigenin, and an inverse ratio of pseudohypericin to hypericin (nearly 1:1 or 1:3) compared to the 1.5:1 or 2:1 ratio characteristically seen in European SJW extracts. The authors attributed these findings to the use of other *Hypericum* species and they point out that spectrophotometric methods for characterizing SJW can be manipulated by adding colorants. The botanical identity of the adulterant *Hypericum* species was not reported.

Meier (2003) noted "Recently, deviations [from the characteristic high-performance liquid chromatography (HPLC) fingerprint of SJW] have been increasingly observed: in the dried herb *H. perforatum* of Oriental origin, especially China, with a botanically definitive identity, rutin is missing.[27] Rutin has been included in the European monograph (Ph Eur) because in a whole series of possible adulterations (other *Hypericum* species) this rutin is missing." Kabelitz

* A systematic review from 2016 including 35 randomized controlled clinical trials on a total of 6993 patients concluded that SJW extracts were superior to placebo and similarly effective to standard antidepressant drugs as a treatment for cases of mild and moderate depression.[5]

(2005) also remarked on the shortage of SJW following the market boom and that "very soon considerable variability of characteristic markers was apparent in the drugs offered for sale."[15] He presented thin layer chromatography (TLC) data showing that rutin was lacking in samples of *H. elegans*, *H. indorum*, *H. maculatum*, and *H. montanum*. However, his chromatograms showed that in samples of "Chinese SJW," rutin was present, and hypericin and/or pseudohypericin were missing.

A chromatographic and spectroscopic study by Huck-Pezzei et al. found that commercial SJW extracts of "Chinese provenance" could be distinguished from products of European origin using TLC, HPLC, and attenuated total reflection mid-range infrared (ATR-MIR) and near infrared spectroscopy (NIR) but not Fourier-transformed infrared (FTIR).[28] TLC chromatograms developed using the European Pharmacopoeia 8.0 (Ph Eur 8.0) method showed that the Chinese samples had an additional orange fluorescent band below hypericin that was not present in the European samples.[29] The European material contained the characteristic 1.5-2:1 ratio of pseudohypericin to hypericin, while the Chinese samples exhibited the inverse (1:2 pseudohypericin:hypericin); therefore, this ratio can be used as an indication for the presence of an alternative species instead of *H. perforatum*. The Chinese samples also contained relatively high amounts of quercetin and low amounts of flavonol glycosides; in many cases, rutin and hyperforins could not be detected by HPLC-UV. The authors concluded that the Chinese samples did not contain SJW but rather another *Hypericum* species. They identified the adulterant species as *H. hirsutum* based on the presence of the compounds kushenols G and H.

The analysis of 37 commercial SJW products using high performance thin-layer chromatography (HPTLC) with the conditions specified in the Ph Eur 8.0,[29] *United States Pharmacopeia* 37 (USP 37),[30] and USP 38[31] identified 14 suspect samples.[25] Eight samples (three commercial dry extracts and five capsules labeled to contain SJW extract) produced a green color when solubilized in methanol (in contrast to the expected red-brown color). Using the conditions specified in USP 38, the corresponding HPTLC chromatograms exhibited four atypical features compared to authenticated reference samples. These findings suggested the presence of other *Hypericum* species and/or the presence of polar compounds not present in authentic SJW samples. A reverse-phase (RP)-HPTLC method was developed to separate and identify the polar additives found at the application position with the USP 38 method. These substances were subsequently determined to be the dyes amaranth, brilliant blue, sunset yellow, and tartrazine. The dyes were present at concentrations ranging from 0.51% and 1.33% among samples from different suppliers, and concentrations also varied among batches from the same source. Overall, the pattern that emerged was a formula of very little tartrazine, roughly equal amounts of amaranth and brilliant blue, and a large quantity of sunset yellow. The authors note that the flavonoid patterns exhibited in these chromatograms were similar to those of the Chinese material described above by Huck-Pezzei et al.[28]

Of the same 37 samples, another six samples (two containing raw herb of Chinese origin, one finished product, and three dry extracts) produced the same atypical chromatograms as the samples adulterated with dyes. However, when these six samples were analyzed using the RP-HPTLC method, no dyes were detected. Microscopic analysis of the raw material samples of Chinese origin revealed the presence of an unknown plant. In a comparative analysis of *H. hirsutum*, *H. montanum*, *H. perforatum*, *H. tetrapterum*, and *H. undulatum* HPTLC chromatograms, the botanical adulterant present in the 14 suspect samples most closely resembled but was not identical to that of *H. undulatum*. It is noted that while the adulterant *Hypericum* species was detected in both raw material and finished product samples, the adulterating suite of dyes were found only in SJW extracts.[25]

Another 2016 study, which evaluated 48 commercial SJW products, also detected dyes in nine of the samples (A. Booker [University College of London] email communication to S. Gafner, August 10, 2016). Seven of the nine products were from the United States, while the other two were sold in the United Kingdom. Adulteration of botanical dietary supplements with dyes has previously been reported with bilberry (*Vaccinium myrtillus*, Ericaceae) fruit[32] and goldenseal (*Hydrastis canadensis*, Ranunculaceae) root and rhizome.[33]

3.2.2 DNA-based evidence: Howard et al. analyzed three commercial SJW products containing dried ground plant material using the polymerase chain reaction (PCR) method and primers to amplify the nuclear ribosomal internal spacer (ITS) sequences.[34,35] DNA from nine of the 490 *Hypericum* species was analyzed and, from these data, the following primers (markers) were selected: a ~750 base pair (bp) "generic" ITS sequence, a 160 bp "genus specific" sequence common to all nine species, and a 80 bp "species-specific" sequence unique to *H. perforatum*. For two of the products, the 160 bp *Hypericum* genus-specific, and 80 bp *H. perforatum* species-specific sequences were obtained, indicating that the products contained SJW. For the third product (an herbal combination containing material from several plant species), the generic ITS region was amplified but was of smaller size compared to SJW and none of the two shorter *Hypericum* specific sequences were amplified, suggesting that amplifiable DNA was present in the sample; however, it was not from *H. perforatum*.

Kazi et al. analyzed 13 commercial SJW products (6 capsules, 5 tablets, and two tinctures) using the same primers as Howard et al.[36] The 80 bp *H. perforatum* species-specific primer was amplified in each of the products, indicating the presence of SJW material. However, only four products (all capsules) yielded amplicons of the longer, generic ITS region, indicating that the DNA in the other nine products was degraded or fragmented.

The botanical identity of the contents of 44 North American single-ingredient commercial herbal products (N = 30 species) was assessed using DNA universal barcoding of

the rbcl and ITS2 regions.[37] Of the three products labeled as "St. John's wort" that were analyzed, one was found to contain barcodes of a Fabaceae species, possibly senna (*Senna alexandrina*, Fabaceae) only and no SJW barcodes. Barcodes for rice (*Oryza sativa*, Poaceae) only were obtained from the second SJW product; the authors suggest that this was possibly due to the use of rice flour as an excipient. SJW barcodes were amplified from the samples of the third SJW product. However, failure to obtain SJW barcodes from two of the SJW products does not necessarily mean the products did not contain SJW; it demonstrates only that SJW DNA was not detected. It should be noted that the veracity and reliability of these findings have been challenged.[38]

Using real-time PCR assays and high resolution melting (HRM) analysis, Costa et al. assessed DNA mini-barcodes for the ITS1 and maturase kinase (*matK*) regions of 13 commercial herbal infusions labeled as containing either *H. perforatum* or *H. androsaemum*. Detectable PCR products were 85 bp or 116 bp for ITS1, and 92 bp for *matK*.[39] One product labeled as containing only *H. androsaemum* also tested positive for *H. perforatum* DNA and another product labeled as containing *H. perforatum* tested positive for *H. androsaemum* DNA. The other 11 products tested positive only for the DNA of the *Hypericum* species indicated on the product label. The confidence level for species identification using HRM was 98.5-99.9%.

3.3 Accidental or intentional adulteration: The botanical identification of SJW is complicated by the significant natural variation observed throughout its range (in both morphological features and chemical profiles), the many features SJW shares in common with the other species in the section Hypericum, and the propensity of SJW to interbreed with these closely-related species to produce intermediate hybrids.[8-10] Given these facts, the reports of frequent adulteration with other *Hypericum* species that are similar in appearance and co-occur within the range of SJW (i.e., *H. barbatum*, *H. hirsutum*, *H. maculatum*, *H. montanum*, and *H. tetrapterum*) are understandable and may be attributed to misidentification or irresponsible wildcrafting.

It seems less likely that adulteration with *H. patulum* or *H. undulatum* may be accidental, because these two species are noticeably different in appearance from SJW and they do not grow in the same native habitats as SJW. Certainly, the adulteration of SJW with other *Hypericum* species and the suite of dyes described by Frommenwiler et al. constitute intentional adulteration.[25]

3.4 Frequency of occurrence: There are no published studies on the frequency of SJW adulteration. The reports by Wichtl[26] and Berghöfer and Hölzl[22] that SJW is frequently adulterated with other *Hypericum* species have been cited by numerous other authors[25,40] and is reiterated on some manufacturer websites.[41] Although corroborating

St. John's Wort *Hypericum perforatum*
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reports are lacking, given the challenges discussed in section 3.3 above, adulteration with other *Hypericum* species can be expected.

The report of frequent substitution of SJW with *H. patulum* by Mitra and Kannan[23] has been repeated (verbatim) by several other authors;[42-44] however, the actual rate of occurrence remains unknown.

Frommenwiler et al. reported that almost 40% of the 37 commercial samples analyzed presented atypical fingerprints indicative of adulteration with other *Hypericum* species and an additional 21% were also adulterated with a suite of synthetic dyes.[25] Booker et al. found 19% of the 48 commercial products tested were adulterated with dyes.

St. John's Wort *Hypericum perforatum*
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3.5 Possible safety/therapeutic issues: The possible safety issues arising from the substitution of SJW with other *Hypericum* species have not been evaluated and few of these species have a history of traditional use as medicines. The potential impact on therapeutic efficacy remains unknown. While several authors have postulated that other *Hypericum* species with chemical profiles similar to SJW may have therapeutic potential, supporting clinical evidence is lacking and it is equally possible that such substitutions may significantly reduce efficacy.[45-47]

Adulteration with dyes poses both safety and legal issues. amaranth is banned in the United States due to the potential toxicity of this dye.[48] Although brilliant blue, sunset yellow, and tartrazine are approved colorants in the United States, they are subject to batch certification by the FDA to ensure they meet the requirements for composition and purity stated in the regulation. "Using uncertified versions of color additives that are subject to FDA certification is illegal in foods, drugs, cosmetics, and medical devices, and will adulterate these products."[49]

Although batch-certified brilliant blue, sunset yellow, and tartrazine are approved colorants in the United States, they have been banned in a number of countries due to safety concerns including behavioral problems in children, carcinogenicity, and exacerbation of asthma and allergies.[50,51] In the European Union, foods containing sunset yellow and tartrazine must carry the additional labeling "may have an adverse effect on activity and attention in children."[52]

The addition of these illegal dyes signals a deliberate effort to mask the substitution of SJW with other *Hypericum* species that do not have a history of safe use and may have decreased or no therapeutic benefits.

3.6 Pharmacopeial standards: The AHP monograph defines SJW as the whole, fresh, or dried plant or its components, containing not less than 0.04% naphthodianthrones of the hypericin group calculated as hypericin.[1] The USP requires not less than 0.04% of hypericin and pseudohypericin combined and not less than 0.6% of hyperforin.[31] The Ph Eur[29] and WHO[2] monographs specify a content of not less than 0.08% total hypericins expressed as hypericin.

Frommenwiler et al. observed that the 14 suspect samples they identified would fail the Ph Eur identity test but would theoretically pass the USP identity test even though an additional zone was present on the latter chromatograms.[25] They propose the addition of the following check to the USP 38 method: in cases where an additional blue zone is observed at the application position, the RP-HPTLC method to detect adulterant dyes should be conducted.

3.7 Analytical methods to detect adulteration: For whole and cut material, botanical identity may be confirmed by a qualified analyst based on organoleptic and macroanatomical characteristics. The identity of powdered material may be determined using a combination of organoleptic, microscopic, and chemical techniques such as TLC or HPTLC. According to Meier, the flavonoid pattern in SJW is quite consistent, making chemical fingerprinting methods a valuable approach to determine identity.[27] There are numerous chemical techniques that may be used to authenticate SJW extracts, including TLC,[22] HPTLC,[25] HPLC-ultraviolet spectroscopy (HPLC-UV), HPLC-mass spectroscopy (HPLC-MS), MIR and NIR spectroscopy,[28] nuclear magnetic resonance (NMR), and various combinations of these methods. The USP and Ph Eur provide official HPTLC and HPLC methods for identification. DNA barcoding techniques may also be used to determine the botanical identity of raw materials; however, the DNA in

some extracts and finished products may be too degraded for reliable identification,[53,54] and additional techniques must be used to confirm that the sample is composed of the correct plant parts.

3.8 Perspectives: Although SJW was been shown to be a safe and effective treatment for mild to moderate depression,[55,56] the market for this herb has been seriously undermined by negative publicity, concerns about alleged and documented adverse herb-drug interactions, and the sale of inferior products that do not have the same chemical profile/potency as the SJW extracts demonstrated as efficacious in clinical trials. The onus (and ability) to restore consumer confidence in the safety, efficacy, and high quality of SJW products rests almost entirely on industry. An independent assessment of the quality of SJW products currently on the market, specifically focused on chemical profiles and phytoequivalency may significantly contribute towards this objective.

It may be questioned whether the reports of "Chinese SJW" with chemical profiles inconsistent with that of "European SJW"[14-15,25,27,28] are in fact cases of adulteration. Although all five articles imply that the "Chinese SJW" samples contained *H. perforatum*, Meier[27] is the only researcher that explicitly stated that the Chinese SJW material was authenticated as *H. perforatum*. Considering the distribution of SJW in China (see section 1.7), the Meier samples most likely contained *H. perforatum* subsp. *chinens*e. The chemical profile of *H. perforatum* subsp. *chinense* has not been reported; however, it is possible that it may constitute a different chemotype from that of the *H. perforatum* subspecies which are distributed in Europe.

However, this chemotype hypothesis does not explain the significant inconsistencies between the chemical profiles ascribed to "Chinese SJW" by the different research groups. Meier stated that rutin is missing in Chinese SJW[27] and Huck-Pezzei et. al.[28] also did not detect rutin in Chinese SJW samples. In contradiction, Kurth and Spreeman[14] stated that Chinese SJW herb and extract had low levels of flavonoids, especially rutin, isoquercitrin, and biapigenin, and Frommenwiler et. al.[25] and Kabelitz[15] demonstrated the presence of rutin in Chinese SJW samples. Kabelitz also showed that pseudohypericin was absent in Chinese SJW. Although pseudohypericin was present in the other Chinese SJW samples,[14,25,27,28] Kurth and Spreeman[14] and Huck-Pezzei et. al.[28] reported that Chinese SJW samples had an inverse ratio of pseudohypericin to hypericin (1:1 or 1:3) compared to "European SJW" which has ratios of 1.5:1 or 2:1.

This variability in the chemical profile of "Chinese SJW" suggests that the different "Chinese SJW" samples contained material from different taxa; some "Chinese SJW" samples may contain *H. perforatum* subsp. *chinense*, or some may contain SJW hybrid(s) or other *Hypericum* species, or some may contain a mixture of SJW and another *Hypericum* species as postulated by Frommenwiler et al.[25] There are 64 *Hypericum* species (33 endemic) found in China, including the closely related species *H. attenuatum* and *H. elegans*, and the reported adulterants *H. hirsutum* and *H. patulum*.[5]

Clearly further research is needed to determine the botanical identity or identities of "Chinese SJW," as well as the chemical profile of *H. perforatum* subsp. *chinense* and its clinical efficacy. However, the fact remains that these "Chinese SJW" samples do not present the same chemical profile as the well-characterized SJW with demonstrated efficacy and do not fulfill the Ph Eur 8.0 and USP 38 identity criteria for SJW.

4 Conclusions

The occurrence of adulteration of SJW with other *Hypericum* species is an ongoing issue that must be addressed with appropriate quality control protocols.

The co-occurrence of adulteration with dyes and other *Hypericum* species raises safety and legal concerns. Industry members are advised to have adequate assays to authenticate their SJW material, and to add an appropriate analytical method to test for dyes to their quality control protocol for SJW extracts.

Research is needed to determine the botanical identity and clinical efficacy (i.e., the wound-healing and antidepressant effects demonstrated with European supplies) of "Chinese SJW."

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REVISION SUMMARY

Version # , Author,	Date Revised	Section Revised	List of Changes
Version 1, A. McCutcheon	n/a	n/a	none