Journal of Ethnopharmacology 158 (2014) 216–220

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jep

Ethnopharmacological communication

Medicinal plants used for respiratory affections in Navarra and their pharmacological validation

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ARTICLE INFO

Article history:
Received 3 July 2014
Received in revised form
2 October 2014
Accepted 4 October 2014
Available online 12 October 2014

Keywords:
Respiratory
Validation
Traditional knowledge
Ethnopharmacology
Navarra

ABSTRACT

Ethnopharmacological relevance: This paper provides important ethnopharmacological information on plants used in respiratory affections in Navarra.
Material and methods: Information was collected using semi-structured ethnobotanical interviews with 667 informants in 265 locations. In order to confirm the pharmacological validation of the uses claimed by the informants, monographs from Official International Agencies (ESCOP, Commission E, WHO and EMA) were reviewed. A literature review was conducted focusing on the plants that were widely used but had no published monograph.
Results: A total of 456 pharmaceutical uses was reported, for 79 plants and 34 families, mainly represented by *Lamiaceae*, *Asteraceae*, *Rosaceae*, *Crassulaceae* and *Malvaceae*. The most frequently used parts were the aerial parts followed by inflorescences and leaves. Twenty-two out of 79 plants (28%) and 270 of 456 uses (42%), had already been pharmacologically validated.
Conclusions: The authors propose *Verbena officinalis* for validation.
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1. Introduction

Traditional medicine is used worldwide and is of great economic importance. In the 21st century, there has been a growing interest in public health in both developed and developing countries. In this sense, traditional medicine has been taking on more and more importance in the eyes of national governments (Bussmann, 2013).

Among the positive aspects of traditional medicine, researchers have pointed to its diversity, flexibility, ease of access, continued acceptance in developing countries and increasing popularity in developed countries, relative low cost, low levels of technological inputs, relatively low side effects and increasing economic importance (Payyappallimana, 2010).

Previous studies carried out by our research group in Navarra showed that two of the ailments commonly treated by traditional medicine are digestive and dermatological diseases (Calvo et al., 2013; Cavero et al., 2013). Following on from this, the aims of the present paper are (i) to conduct a scientific validation of the medicinal plants used for respiratory affections, and (ii) to propose *Verbena officinalis* for further scientific validation.

2. Methodology

Information was collected using semi-structured ethnobotanical interviews with 667 informants in 265 locations (Navarra, Spain) following the methodology described in previous papers (Calvo et al., 2011; Cavero et al., 2011a, 2011b).

In order to confirm the pharmacological validation of the uses claimed by the informants, monographs from Official International Agencies (ESCOP, Commission E, WHO and EMA) were reviewed. A literature review was carried out for the plants that were reported to be in widespread use, for which no monograph exists (Calvo et al., 2013; Cavero et al., 2013).

3. Results and discussion

A total of 456 pharmaceutical uses was reported, belonging to 79 plants (81% native and 19% introduced species from other continents, or other European regions). The complete catalog of the ethnoflora of the surveyed territory is given in Akerreta (2009).

The 79 medicinal plants belong to 34 families, mainly represented by *Lamiaceae* (15%), *Asteraceae* (13%), *Rosaceae* (9%), *Crassulaceae* and *Malvaceae* (5% each), and *Boraginaceae*, *Fabaceae*, *Fagaceae* and *Scrophulariaceae* (4% each).

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http://dx.doi.org/10.1016/j.jep.2014.10.003
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Table 1
Plants with pharmacological validation

Plant (family, voucher specimen)	Part used	Ph	Preparation	Popular use (FU)	Monograph
Agrimonia eupatoria L. ssp. *eupatoria* (*Rosaceae*, 21932)	Aerial part, leaf		Infusion, gargle with infusion	Sore throat (6)	1[a], 2, 4[a]
	Flowered aerial part	A, B	Gargle	Sore problems (2)	1, 2, 4
Allium sativum L. (*Liliaceae*, 21718)	Bulb	A, B	Poultice with boiled in wine, comestible	Catarrh, pneumonia (3)	1
Althaea officinalis L. (*Malvaceae*, 18805)	Flower		Infusion	Catarrh (1)	1[a], 2[a], 3[a], 4[a]
	Root	A	Vapors with infusion	Sore throat (1)	1, 2[a], 3, 4
	Whole plant		To breathe	Sore problems (1)	1[a], 2[a], 3[a], 4[a]
Calendula officinalis L. (*Asteraceae*, 18787)	Inflorescence	A, B	To chew, ointment with wax and olive oil	Sore throat (2)	1, 2, 4
Chelidonium majus L. (*Papaveraceae*, 21859)	Aerial part	A, B	Decoction	Bronchial problems (1)	4
Eucalyptus globulus Labill. (*Myrtaceae*, 18799)	Leaf petiole	A, B	Vapors with infusion, sirup	Catarrh (4)	1[a], 2[a], 3, 4
Glycyrrhiza glabra L. (*Fabaceae*, 21523)	Rhizome	A	Maceration in wine, to chew	Bronchitis, catarrh, sore throat (3)	1, 2, 3, 4
Malva sylvestris L. (*Malvaceae*, 21825)	Whole plant		Decoction, comestible	Expectorant (2)	1[a], 2[a]
	Aerial part, leaf	A, B	Decoction, infusion, boiled in poultice, comestible	Catarrh, colds, bronchial problems (9)	1[a], 2[a]
			Decoction, vapors with decoction, infusion	Diseases of the respiratory tract, sore problems, colds, bronchial problems, cough (8)	1[a], 2[a]
	Flowered aerial part	A	Vapors with decoction	Cleaning airways (1)	1[a], 2[a]
	Flower	A	Vapors, infusion, decoction, sirup	Catarrh (7)	1, 2
Marrubium vulgare L. (*Lamiaceae*, 18686)	Aerial part	A, B	Infusion, decoction	Bronchitis, diseases of the respiratory tract, cough (3)	4
Mentha aquatica x *Mentha spicata* (*Lamiaceae*, 21646)	Stem, leaf	A, B	Infusion	Diseases of the respiratory tract (1)	4[a]
Origanum vulgare L. (*Lamiaceae*, 21640)	Inflorescence		Infusion, decoction	Catarrh, pneumonia (6)	2
Pinus sylvestris L. (*Pinaceae*, 18798)	Leaf		To breathe, vapors with decoction	Bronchial problems (2)	2[a]
	Bud		Decoction, infusion	Bronchodilator, catarrh (3)	2
Plantago lanceolata L. (*Plantaginaceae*, 18713)	Stump-Rhizome		Decoction	Bronchitis (1)	1[a], 2[a], 4[a]
	Aerial part		Poultice, decoction	Sore throat (2)	1, 2, 4
	Leaf	A, B	Sirup, poultice with decoction	Catarrh (2)	1, 2, 4
			Heat the juice with honey and direct application, poultice with hot leaves	Bronchitis, cough (3)	1, 2, 4
			Infusion	Prevention of colds (1)	1, 2, 4
Prunus spinosa L. (*Rosaceae*, 21969)	External bark		Vapors with decoction	Catarrh (1)	2[a]
	Fruit		Decoction with brandy and honey	Catarrh (1)	2
Quercus coccifera L. (*Fagaceae*, 21534)	External bark, leaf		Infusion	Tonsillitis (1)	4
Quercus humilis Mill. (*Fagaceae*, 21538)	Trunk, branch		Poultice with ash in hot water	Sore throat (1)	4
Rosa agrestis Savi (*Rosaceae*, 21970)	Flower		Maceration in anisette, infusion, vapors with infusion	Catarrh (4)	2
	Fruit		Decoction, infusion	Cough, catarrh (3)	2[a]
Rosa canina L. (*Rosaceae*, 18809)	Flower		Maceration in anisette, infusion, vapors with infusion	Catarrh (4)	2
	Fruit	A, B	Jam	Sore throat (2)	1, 2[a]
			Infusion	Catarrh (2)	2[a]
Sambucus nigra L. ssp. *nigra* (*Adoxaceae*, 18661)	Internal bark		Infusion, ointment with lard and wax	Catarrh (2)	2[a], 3[a], 4[a]
	Leaf		Poultice with roasted leaves	Sore throat (1)	2[a], 3[a], 4[a]
	Inflorescence	A, B	Decoction and/or infusion with milk, vapors, infusion	Catarrh (28)	2, 3, 4
			Smoke inhalation, poultice, infusion, sirup, heated and direct application, vapors	Sore throat, diseases of the respiratory tract: congestion, to the chest (13)	2, 3, 4
	Fruit	A	Jam	Catarrh (1)	2[a], 3[a], 4[a]
Thymus vulgaris L. (*Lamiaceae*, 21713)	Leaf	A, B	Crushed and direct application	Occlusion of the ear by earwax (1)	1, 2, 3, 4
	Aerial part	A, B	Gargle with decoction, decoction, infusion, vapor with infusion	Catarrh, bronchial problems, sore throat, bronchitis (28)	1, 2, 3, 4
	Flowered aerial part	A, B	Infusion, gargle with infusion	Catarrh, bronchitis, expectorant, sore problems (16)	1, 2, 3, 4
Tussilago farfara L. (*Asteraceae*, 18652)	Leaf		Infusion	Catarrh (1)	2
Verbascum thapsus L. (*Scrophulariaceae*, 18731)	Leaf		Infusion	Diseases of the respiratory tract, catarrh (4)	2[a], 4[a]
	Aerial part		Infusion	Catarrh (1)	2[a], 4[a]
			Direct application with maceration in oil	Otitis (1)	2[a], 4[a]

Ph: Pharmacopeia; A: European Pharmacopoeia; B: Real Farmacopea Española; FU: frequency of uses; 1: ESCOP monograph; 2: German Commission E monograph; 3: WHO monograph; and 4: EMA monograph.

[a] Different parts used.

The most frequently used parts of the plants were its aerial parts (39%), inflorescences (13%), leaves (12%), flowered aerial parts (9%), fruits (8%), bulbs (5%), flowers (4%) and the whole plant (2%).

Plants were used fresh (44%), dry (28%), or either (27%) and lost knowledge (1%) for administration in different forms. The percentage of internal uses was three times higher than that for external uses (67% and 33%, respectively), and the most important forms of preparation were infusion (44%), decoction (15%), vapors (12%), gargle (7%), and maceration (6%); in lower proportions, juice (4%), jump (3%) and edible parts (2%); for external uses, poultices (87%) were used, the principal excipients being eggwhite (67%).

Twenty-two out of 79 plants (28%) and 270 of 456 popular uses (42%) had already been pharmacologically validated for respiratory affections by ESCOP, Commission E, WHO and EMA Monographs (Table 1). It is important to highlight that seven of twenty-two plants already had monographs in the four agencies taken into consideration.

Ten out of twenty-two plants (45%) listed in Table 1 had no monograph in the European Pharmacopoeia and/or Real Farmacopea Española.

The remaining plants (57, 72%) have been reported for respiratory troubles and need to be screened through standard scientific procedures for their actions. Taking into consideration only the uses mentioned by two or more independent informants (212 uses, Table 2), we found that the most widely treated affections fell into seven pathological categories: antitussive (6%), bronchi and lung (23%), catarrh (32%), ear (9%), prevention of colds (6%), sinusitis (8%), and throat (16%).

The onion plant (*Allium cepa*) is used as a vegetable and is the most widely cultivated species of the genus *Allium*. In this study, the results showed that *Allium cepa* is employed as an antitussive agent (13 out of 212 total uses, 6%). The bulbs cut in pieces or poultices are employed to prevent coughing at night.

The most common problem with the bronchi is bronchitis, an inflammation of the tubes. Seven plants were cited for treating this, four of them (*Cynoglosum officinale*, *Symphytum* sp., *Triticum aestivum* and *Verbena officinalis* (40 uses of 47 total uses)) being administered externally in poultices.

The flowered aerial parts of *Salvia verbenaca* were used as an expectorant, defined as an agent which produces an increase of the bronchial mucus secretions facilitating their expulsion (Blumenthal et al., 1998).

Catarrh, defined as an inflammation of a mucous membrane of the respiratory tract, was the most cited affection (15 plants, 67 out of 212 total uses). The most widely employed plants were *Verbena officinalis* (39%, 26 uses), *Agrimonia eupatoria* and *Allium cepa* (9%, 6 uses each).

Drops of the leaf crushed from *Hylotelephium telephium* by direct application (26%, 5 out of 19 total uses) and oil maceration of *Hypericum perforatum* (21%, 4 uses) were used for earache and otitis.

The fruits of genus *Rosa* are best known for their high content of vitamin C (Tumbas et al., 2012) and are one of the most commonly consumed in this region for the prevention of colds (6 uses in maceration with anisette, 5 uses in jam).

The inflammation of the paranasal sinuses, a disease known as sinusitis, can be due to infection, allergy, or autoimmune problems. Most cases are due to a viral infection and resolve over the course of 10 days (Anon, 2010). A poultice of *Verbena officinalis* using eggwhite as excipient is well known as the famous “verbena omelette” for this affection (Cavero et al., 2011a). In this study, 17 out of 212 total uses (8%) were reported.

Decoction of *Phlomis lychnitis* to treat aphonia was frequent (6%, 2 out of 34 total uses for this affection), as was the poultice of *Verbena officinalis* (26%, 9 uses) and *Triticum aestivum* (24%, 8 uses) for sore throat and tonsillitis.

In summary, it is important to highlight that the most widely cited plant for respiratory problems was *Verbena officinalis*. It appeared in five out of eight affections analyzed (42%, 89 out of 212 total uses).

Verbena officinalis, commonly known as vervain and verbena, is a perennial plant which grows wild throughout much of Europe and North Africa, as well as in China and Japan. This herb has been used as folk medicine for thousands of years for the treatment of abdominal mass, amenorrhea, dysmenorrhea, malaria, pharyngitis, carbuncles, edema, etc.

Regarding respiratory affections, a review of literature from etnopharmacological studies has showed that *Verbena officinalis* is used in different regions of Spain: Andalusia, Basque Country, Canary Islands, Cantabria, Catalonia, Navarra, Principality of Asturias and Valencian Community (Akerreta, 2009, and references cited therein; Cavero et al., 2011a, 2011b; Menendez-Baceta et al., 2014). Additionally, two ethnopharmacological references were found in other areas: Federal Democratic Republic of Ethiopia (Teklehaymanot and Giday, 2007) and Republic of Serbia (Jarić et al., 2007).

In 1990 Commission E published an unapproved monograph about *Verbena officinalis* because its activity for respiratory problems (diseases and ailments of the oral and pharyngeal mucosa, such as tonsillitis, sore throats, and diseases of the respiratory tract, such as cough, asthma and whooping cough) had not been adequately proven. However, the same monograph indicates that because of its secretolytic action, it is possible that the plant can contribute positively to the activity of established combinations for use in catarrhs of the upper respiratory tract (Blumenthal et al., 1998).

Since 1990, studies on its pharmacological activities have mainly focused on the anti-inflammatory and analgesic (Calvo, 2006), antioxidant (Rehecho et al., 2011), antitussive (Ren et al., 2013) effects as well as its antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (Ahmed et al., 2012). The main chemical constituents include iridoid glycosides, such as verbenalin and its derivatives hastatoside and aucubin, verbenoside A and B, gentiopicroside and flavonoid compounds, ursolic acid, volatile oils and terpenoids (Bilia et al., 2008; Rehecho et al., 2011). These constituents could be responsible for some of the above mentioned effects.

Verbena officinalis has been approved as a herbal medicine and dietary supplement by regulatory bodies in many countries (Lai et al., 2006). In Spain, it is possible to find this herb in simple formulations (dried and pulverized plant, mainly) or in a fixed combination, Sinupret®, for respiratory problems. Sinupret® (manufactured by Bionorica, Neumarkt, Germany) is an aqueous-ethanolic extract from five plants, *Gentiana lutea* L., *Primula veris* L., *Sambucus nigra* L., *Rumex acetosa* L. and *Verbena officinalis* L., frequently used in the treatment of acute and chronic rhinosinusitis and respiratory viral infections such as the common cold. Pharmacological studies employing in vitro and animal models have found that Sinupret® has antimicrobial and antiviral effects, secretolytic activity (breaks down secretions, reduces the viscosity of mucus) and anti-inflammatory activity. All of these actions are important for treating respiratory infections (Glatthaar et al., 2009).

Pharmacological and phytochemical studies described above could provide the basis for preparing a paper to validate the safety and efficacy of this herb for approval by Official International Agencies.

4. Concluding remarks

Twenty-eight percent of the medicinal plants used in Navarra for respiratory problems have been pharmacologically validated by Official International Organisms. Of the remaining 72%, the authors

Table 2
Plant without pharmacological validation (mentioned by two or more independent informats).

Affection	Plant (Family, voucher specimen)	Part used	A[a]	Preparation (number of use reports)	FU[b]	TFU[c]
Antitussive	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	External (F)	Bulb is cut into pieces and placed next to the bed (10), poultice (3)	13	
						13
Bronchi and lung						
Bronchial problems	*Cynoglossum officinale L.* (*Boraginaceae*, 21119)	Aerial part	Internal (I), External (I)	Poultice (1), decoction (1)	2	
	Lavandula latifolia Medicus (*Lamiaceae*, 21581)	Inflorescence, leaf	Internal (D, I)	Decoction (1), infusion (1)	2	
	Pulmonaria longifolia (Bast.) Boreau (*Boraginaceae*)	Whole plant	Internal (F)	Infusion (2)	2	
	Symphytum sp. (*Boraginaceae*, 21134)	Root	External (F)	Poultice with two eggwhites (2)	2	
	Triticum aestivum L. (*Poaceae*, 18797)	Fruit (seed)	External (I)	Poultice with roasted fruit (2)	2	
	Verbena officinalis L. (*Verbenaceae*, 21770)	Aerial part, Leaf	External (D, F, I)	Poultice (35)	35	
	Vitis vinifera L. (*Vitaceae*, 21808)	Fruit	Internal (F)	Decoction with wine, lard and honey(1), Decoction with wine (1)	2	
						47
Expectorant	*Salvia verbenaca* L. (*Lamiaceae*, 21679)	Flowered Aerial part	Internal (F), External (F)	Infusion (1), poultice (1)	2	
						2
Catarrh	*Agrimonia eupatoria* L. ssp. *eupatoria* (*Rosaceae*, 21932)	Leaf, Aerial part	Internal (F, I)	Infusion (3), gargles with infusion (3)	6	
	Allium cepa L. (*Liliaceae*, 19324)	Bulb	Internal (F), External (F)	Juice (1), maceration in water and honey (1), decoction with milk (1), decoction (2), poultice with oil (1)	6	
	Anagallis arvensis L. (*Primulaceae* 19649)	Whole plant, Flowered Aerial part	Internal (I)	Infusion (2)	2	
	Artemisia herba-alba Asso (*Asteraceae*, 21201)	Flowered Aerial part	Internal (D)	Vapors (2)	2	
	Cynoglossum officinale L. (*Boraginaceae*, 21119)	Aerial part	Internal (I), External (I)	Poultice (1), decoction (1)	2	
	Galium verum L. ssp. *verum* (*Rubiaceae*, 21992)	Aerial part, Whole plant	Internal (I)	Infusion (1), decoction (1)	2	
	Jasonia glutinosa (L.) DC. (*Asteraceae*, 21271)	Flowered Aerial part	Internal (D)	Infusion (2)	2	
	Jasonia tuberosa (L.) DC (*Asteraceae*, 21275)	Flowered Aerial part	Internal (D)	Infusion (2)	2	
	Santolina chamaecyparissus L. ssp. *squarrosa* (DC.) Nyman (*Asteraceae*, 18777)	Inflorescence	Internal (D)	Infusion (4)	4	
	Trigonella foenum-graecum L. (*Fabaceae*, 21140)	Fruit	External (D)	Poultice with flour fruit and water (2)	2	
	Triticum aestivum L. (*Poaceae*, 18797)	Fruit (seed)	External (I)	Poultice with roasted fruit (5)	5	
	Urtica dioica L. (*Urticaceae*, 19663)	Aerial part	Internal (F, I)	Infusion (1), vapor (1), vapor with decoction (1)	3	
	Verbascum sinuatum L. (*Scrophulariaceae*, 22009)	Leaf	Internal (I)	Infusion (2)	2	
	Verbena officinalis L. (*Verbenaceae*, 2177)0	Aerial part, Leaf	External (F, I)	Poultice with eggs (26)	26	
	Viola riviniana Rchb. (*Violaceae*, 18808)	Aerial part	Internal (I)	Infusion (1)	1	
						67
Ear (earache, otitis)	*Chamaemelum nobile* (L.) All. (*Asteraceae*, 21222)	Inflorescence	Internal (D)	Warmed with oil and direct application (2)	2	
	Hylotelephium telephium (L.) H. Ohba (*Crassulaceae*, 19677)	Leaf	Internal (F)	Juice (5)	5	
	Hypericum androsaemum L. (*Clusiaceae*, 21551)	Flowered Aerial part	Internal (F)	Maceration in oil (2)	2	
	Hypericum perforatum L. (*Clusiaceae*, 21555)	Flowered Aerial part	Internal (F, D)	Maceration in oil (4)	4	
	Sedum sp. (*Crassulaceae*, 19885)	Leaf	Internal (F)	Crushed (3)	3	
	Umbilicus rupestris (Salisb.) Dandy (*Crassulaceae*, 21347)	Leaf, Aerial part	Internal (F)	Direct aplication (3)	3	
						19
Prevention of colds	*Rosa agrestis* Savi (*Rosaceae*, 21970)	Fruit,	Internal (F)	Infusion (1), comestible (1), maceration in anisette (3), Jam (2),	7	
	Rosa canina L. (*Rosaceae*, 18809)	Fruit,	Internal (F)	Jam (3), maceration in anisette (3)	6	
						13
Sinusitis	*Verbena officinalis* L. (*Verbenaceae*, 2177)0	Aerial part, Leaf	External (D, F, I)	Poultice with eggs (17)	17	
						17
Throat						
Aphonia	*Phlomis lychnitis* L. (*Lamiaceae*, 21643)	Leaf	Internal (D)	Decoction (2)	2	

Table 2 (*continued*)

Affection	Plant (Family, voucher specimen)	Part used	A[a]	Preparation (number of use reports)	FU[b]	TFU[c]
Antitussive	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	External (F)	Bulb is cut into pieces and placed next to the bed (10), poultice (3)	13	
						13
Sore throat	*Achillea millefolium* L. ssp. *millefolium* (*Asteraceae*, 21185)	Inflorescence	Internal (D)	Vapors with decoction (3)	3	2
	Anagallis arvensis L. (*Primulaceae*, 19649)	Aerial part, Whole plant	Internal (D, Lk)	Infusion (2)	2	
	Citrus limon (L.) Burm. (*Rutaceae*, 21189)	Fruit	Internal (F), External (F)	Juice with honey (2), maceration in alcohol with a lemon (1)	3	
	Salvia verbenaca L. (*Lamiaceae*, 21679)	Leaf, Flowered Aerial part	Internal (D, I)	Gargles with infusion (2), infusion (1)	3	
	Triticum aestivum L. (*Poaceae*, 18797)	Fruit (seed)	External (D, I)	Poultice with roasted fruit (4), poultice with wine decoction (1)	5	
	Verbena officinalis L. (*Verbenaceae*, 2177)0	Aerial part	External (F), Internal (F)	Poultice with eggs (7), infusion (1)	8	
						24
Tonsillitis	*Triticum aestivum* L. (*Poaceae*, 18797)	Fruit (seed)	External (D, I)	Poultice with eggs or with oil (2), poultice with roasted fruit (1)	3	
	Urtica dioica L. (*Urticaceae*, 19663)	Aerial part	Internal (I)	Vapors (2)	2	
	Verbena officinalis L. (*Verbenaceae*, 2177)0	Aerial part	External (F), Internal (F)	Infusion (1), poultice (2)	3	
						8

[a] A: Administration; F: fresh; D: dry; and I: without distinction.
[b] FU: Frequency of uses.
[c] TFU: Total frequency of uses.

highlight *Verbena officinalis* for its validation. Numerous ethnobotanical, phytochemical and pharmacological studies suggest that this medicinal plant is proved to be effective for respiratory problem and can be used after its validation for further refinement and improvement, which might lead to relatively inexpensive, effective and safe therapies.

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