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Are the Correct Herbal Claims by Hildegard von Bingen Only Lucky Strikes? A New Statistical Approach

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Keywords
Statistical method · History of medicine · Herbal claims · Herbal medicine · Phytotherapy · Hildegard von Bingen

Summary
Background: Ancient and medieval herbal books are often believed to describe the same claims still in use today. Medieval herbal books, however, provide long lists of claims for each herb, most of which are not approved today, while the herb's modern use is often missing. So the hypothesis arises that a medieval author could have randomly hit on 'correct' claims among his many 'wrong' ones. **Methods:** We developed a statistical procedure based on a simple probability model. We applied our procedure to the herbal books of Hildegard von Bingen (1098–1179) as an example for its usefulness. Claim attributions for a certain herb were classified as 'correct' if approximately the same as indicated in actual monographs. **Results:** The number of 'correct' claim attributions was significantly higher than it could have been by pure chance, even though the vast majority of Hildegard von Bingen's claims were not 'correct'. The hypothesis that Hildegard would have achieved her 'correct' claims purely by chance can be clearly rejected. **Conclusion:** The finding that medical claims provided by a medieval author are significantly related to modern herbal use supports the importance of traditional medicinal systems as an empirical source. However, since many traditional claims are not in accordance with modern applications, they should be used carefully and analyzed in a systematic, statistics-based manner. Our statistical approach can be used for further systematic comparison of herbal claims of traditional sources as well as in the fields of ethnobotany and ethnopharmacology.

Schlüsselwörter
Statistische Methode · Medizingeschichte · Indikationsangaben · Heilpflanzen · Phytotherapie · Hildegard von Bingen

Zusammenfassung
Hintergrund: Man geht oft davon aus, dass alte Kräuterbücher dieselben Indikationen angeben, wie die heute üblichen. Kräuterbücher aus dem Mittelalter geben jedoch lange Indikationslisten für jede Pflanze an, von denen die meisten heute nicht mehr anerkannt sind, und oft fehlt sogar die heutige Indikation. So drängt sich die Hypothese auf, dass ein mittelalterlicher Autor die «richtige» Indikation unter den vielen «falschen» rein zufällig angegeben haben könnte. **Methoden:** Wir entwickelten ein statistisches Verfahren auf der Basis eines einfachen Zufallsmodells. Wir wandten das Verfahren beispielhaft an den Kräuterbüchern von Hildegard von Bingen (1098–1179) an und klassifizierten deren Indikationszuweisung zu einer Pflanze als «richtig», wenn sie in etwa den heutigen Monographien entsprach. **Ergebnisse:** Die Zahl der «richtigen» Indikationsangaben lag signifikant höher als durch Zufall erwartet werden kann, obwohl die Mehrheit der Indikationsangaben heute nicht als «richtig» anerkannt ist. Die Hypothese wird klar widerlegt, dass Hildegard von Bingen ihre «richtigen» Indikationsangaben durch Zufall getroffen haben kann. **Schlussfolgerung:** Der nicht durch Zufall erklärbare Zusammenhang zwischen den Indikationsangaben eines mittelalterlichen Autors mit heutigen Indikationsangaben stützt die Bedeutung traditioneller Medizinsysteme als empirische Quelle. Aber da viele traditionelle Indikationsangaben nicht mit modernen Anwendungen übereinstimmen, sollten sie mit Vorsicht herangezogen und in einer systematischen, statistikbezogenen Weise ausgewertet werden. Unser statistischer Ansatz kann für weitere systematische Vergleiche von traditionellen Angaben sowie im Gebiet der Ethnobotanik und Ethnopharmakologie verwendet werden.

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Introduction

The common belief among patients using complementary and alternative medicine (CAM) that herbal medicines are based mainly on traditional knowledge is fed by publications describing how the same use (indication) of a plant that modern herbalists recommend today would be mentioned by many ancient herbal books. Ancient and medieval books from Europe, however, provide long lists of claims for each herb – to be understood within the context of humoralism – and often cover several organ systems. Hence, their information would appear to be far less specific. However, many publications about the history of herbal therapy focus on picking out only those claims that are of interest today.

An interdisciplinary approach was adopted to develop a statistical procedure to test the hypothesis that a medieval author may just have randomly hit on some 'correct' (modern) indications. We applied this method to the medicinal books of Hildegard von Bingen (1098–1179) [1–3] as an example. The famous German abbess, author of literature on many topics, provides detailed descriptions of diseases and symptoms to be treated by a considerable number of plants, and it is easy to understand which claims were intended. Her claims and also her descriptions seem not too deeply influenced by the context of humoralism. Furthermore, she is not listing all the claims ever mentioned by ancient authorities, and so her claim attributions seem rather independent.

Material and Methods

Our statistical approach is based on the model of the game Battleship where a two-dimensional grid (similar to an Excel spreadsheet) is formed by all the claims known to the author on one axis and the herbs (those still used today) on the other axis. Modern herbal indications (medical uses) are represented as 'ships' which the medieval author tries to hit by randomly tossing a 'missile' into the grid. The hypergeometric distribution gives the probability that x 'correct' indications ('hits') could be drawn from the set of N herb/claim combinations with n 'shots', and the number of 'ships' (today's herb/claim attributions) is M.

It would be unfair to use today's classification systems for nosology such as the International Classification of Diseases (ICD), since a medieval author could not have known diseases such as acquired immunodeficiency syndrome (AIDS) or syphilis. He could also not have known diseases such as arterial hypertension, which show no apparent clinical symptoms. Therefore, the total number of symptoms/diseases has to be outnumbered by all available texts in this context to get an approximation for those symptoms/diseases known to the author (and regarded worthwhile as subjects for a therapy mentioned in his/her book). Another approach is to classify each symptom into only 15 organ-related classes to answer the question of whether the organ targeted by a treatment would have been stable over the centuries and ignoring changes of claims within that organ.

Those plants which are no longer in use today for poisonous effects and which would therefore no longer have any indications (e.g., *Ligustrum vulgare*, *Heleborus niger*, *Conium maculatum*) (Group 2) were excluded from the statistical analysis. It would be unfair to the author to judge his/her claims related to these plants as 'wrong'. Instead it seems preferable to focus on those plants that are still in use today as herbal medicines (Group 1). Also plants that are no longer regarded as pharmacologically active but are used as foods without specific medical claims, such as apples, figs, citrus fruits etc. (Group 3), should be treated with caution or excluded.

Finally, each claim attribution made by the author was judged as to its conformity with modern indications according to current knowledge ('hit') (versus nonconformity = 'miss'). Formally, a 'correct' claim ('hit') was defined as one still valid today according scientific monographs of Commission E [4] or the European Scientific Cooperative on Phytotherapy (ESCOP) [5], as performed and presented in detail in a thesis some years ago (at a time when EMEA monographs were not yet available) [6]. In unclear cases, Bernhard Uehleke and a number of colleagues with historic and botanical expertise were consulted (Forschungsgruppe Klostermedizin, University of Würzburg, Germany).

Results

Symptoms/Diseases Known to Hildegard von Bingen

We systematically dissected Hildegard von Bingen's available texts [7, 8] to approximate the set of different symptoms/diseases known to her. A detailed list of symptoms/diseases made sense, since she had provided detailed symptoms. The syndrome known today as the 'common cold' would include several symptoms such as cold limbs, cough, hoarseness, etc. Claims with different wording but identical meaning were summarized as 1 symptom/disease, resulting in 115 different symptoms/diseases. Another approach was to classify the claims into only 15 organ-related classes.

Plants Used for the Analysis

We focused on those 85 plants that are still used as herbal medicines today (Group 1). We excluded plants with poisonous effects (Group 2) that are no longer used (although eventually their isolated substances may be used), because it would have been incorrect to have considered indications for plants in Group 2 as purely 'wrong'. Group 3 included 90 plants that are no longer regarded as pharmacologically active but are used as foods without medical claims. We also applied the statistical procedure to Groups 1 and 3 in combination (175 plants).

Claim Attributions: 'Hits' and 'Misses'

Hildegard von Bingen gave 437 claim attributions ('shots') to 175 plants (or to the grid of 20,125 claim/plant combinations) and 212 to 85 plants of Group 1 (9,775 combinations) still used for medicinal purposes today. Both grids contain 310 modern indications ('ships'). Her 407 'misses' on 175 plants and 182 'misses' on 85 herbs very much outnumbered her 30 hits. A systematic extraction of basis data from the ancient sources was performed by Bernhard Uehleke and Christine Mayer-Nicolai; detailed data are provided in her thesis [6]. The expected value for Hildegard von Bingen's hits is 6.73 for 437 shots on 175 plants and 6.72 for 212 shots on 85 plants. Hence, her 30 hits exceed the probable random hits by a fac-

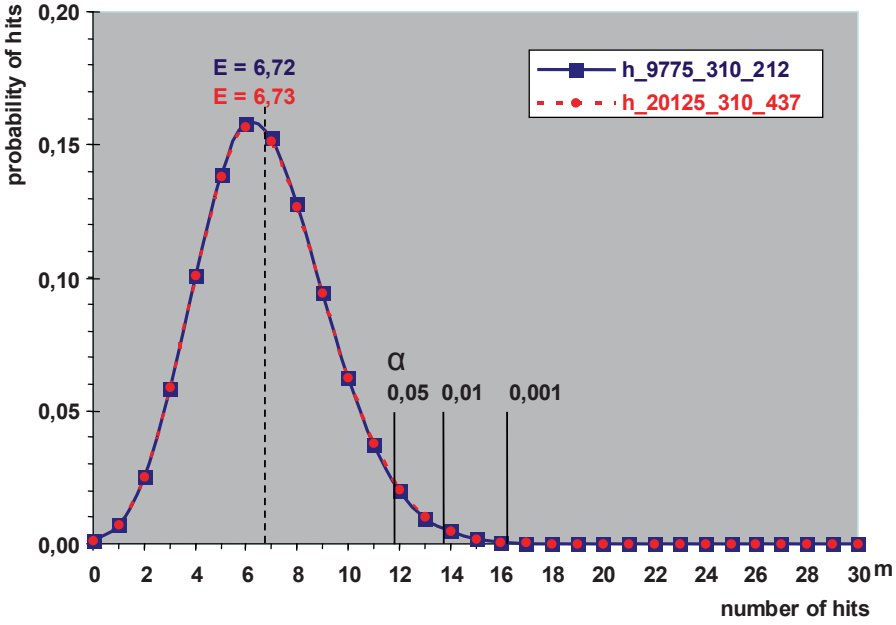

Fig. 1. Hypergeometric distribution: probability to have hits in a battleship with 310 ships on a grid of N = 9,775 (or 20,125, respectively) fields with 212 (or 437, respectively) shots; α represents the chance to be outside of the area under the curve (e.g. chance of 17 hits or more is below α = 0.001) [10].

tor of more than 4. Both distribution curves (fig. 1) show that the probability of 30 hits (or more) being achieved by chance is below 10^{-7}. Using the grid of only 15 organ-related claims, Hildegard had 35 'correct' hits. The probability of achieving 35 hits by chance is still below 10^{-3}.

Discussion

A similar random model is inherent in each multiple-choice test: in a test offering 5 possible answers, a student is expected to have many more hits than those 20% expected to occur by chance to pass the exam. In some tests, false answers are counted as negative points; however, we did not take this approach, since in most cases there is no explicit clinical evidence that a 'false' claim of an ancient or medieval author on a herb no longer in use is really 'not working'. Therefore, one could speculate that at least some of the many 'false' claim attributions (misses) by Hildegard von Bingen could switch to hits after new research.

The hypothesis that Hildegard could have achieved her 'correct' claims by chance is to be clearly rejected on the basis of the highly significant level of our new statistical procedure. The finding from this approach that medieval medical claims are significantly correlated with modern herbal indications supports the importance of traditional medicinal systems as an empirical source.

With a more unspecific interpretation of Hildegard's organ-related claims, the number of hits (within the same organ claim spectrum) is still significantly greater than it could be by chance. However, if the organ targets were to be expanded by pharmacological considerations, one could enter into a range where the situation changes (many ships in a coarse grid with few squares are then easy to hit). Our results are stable with respect to a more or less strict evaluation: even when much more modern indications would be regarded as correct than those few given by the monographs [4, 5] for each herb, the corresponding higher rate of hits to the greater number of ships could still not be explained by chance.

It may be worth reflecting on the reasons why modern monographs restrict themselves to 1 or only few indications for each plant. The multi-component mixture of active ingredients in herbs might support further claims for many herbs. However, the reason for the establishment of the Commission E monographs was to provide an easier procedure for re-registration of herbal products registered in Germany as drugs according to the high standards of German and European drug legislation. For this procedure, monographing a second claim would have had the consequence that manufacturers could get an easy extension of their claims, which was not intended politically. This is the pragmatic reason for the fact that most Commission E monographs, and subsequently ESCOP monographs and HMPC (Committee on Herbal Medicinal Products) monographs, are restrict to 1 or only few indication claims. Prior to the work of Commission E, the range of indications applied by the manufacturers of a certain plant was only somewhat broader, so it was easy to identify the 1 indication for which the collected materials provided the best evidence (including preclinical (plausibility) and clinical studies and experience). This kind of selection process of claims might be worth reconsidering on a more scientific rather than pragmatic basis.

Another process of selecting certain claims from long indication lists of medieval sources occurred at an earlier time around the 19th century during the paradigm shift from humoralism to organ- and cell-related thinking in medicine.

Since doubts may be justified that this process of selecting old claims or eventually adding new claims based on new pharmacological and other insights was based on proper scientific reasoning, it may be worth reconsidering also this process (as well as that of the Commission E described above) and eventually repeat both selection processes on a more solid basis. It is important to realize that European herbal medicine is characterized by restriction to certain plants with good tolerability only and then by constraints in the range of claims for each single plant.

Our statistical approach gives input to research into how therapeutic traditions can lead to modern use. The assumption that generations of healers would have experimented with a wide variety of herbs and indications and then narrowed them down after observing what worked best should be reconsidered. Healers would have had to observe hundreds or thousands of herb/indication attributions. Taking into account the variability of treatments in individual patients, this explanation is doubtful. We suggest a subanalysis of herbs with rapid-onset effects versus herbs with late-onset effects to clarify these questions. Our statistical method is quite forward compared to other quantitative approaches such as that adopted by Leonti et al. [9] using Bayesian statistical inference in ethnopharmacy. Our method can be used analogously to test for concordance/overlap between 2 or several sources (e.g. herbal books). It can be used for testing for differences or concordances in time from region to region, and from source to source, or author to author in the fields of CAM and medical history as well as in ethnopharmacology.

Conclusion

We provided an example of how statistical methods can be used for testing hypotheses about the validity of information from traditional sources. Our new statistical approach can be used to test hypotheses and to compare claim attributions from various sources. The usual narrative describing how some traditional sources would assign a certain therapeutic indication without any critical discussion or statistical consideration is likely to develop bias.

Acknowledgement

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Disclosure Statement

None of the authors declare any conflict of interest.

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