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1. A. The science of zoopharmacognosy, where do we stand? (1)
Tedje van Asseldonk, IEZ, NL (info@ethnobotany.nl)

Abstract
The first documented observations of animals using medicinal herbs are about 2000 years old, but this type of animal behavior was neglected in new science until the recent 90's. Still nowadays it's difficult to locate systematic research, although there's a lot of anecdotal observations in this field. The interpretation of these observations is still under discussion as are the scientifically valid methods that could help to shed more light on these interesting phenomena.

Introduction
The Netherlands (NL) Institute for Ethnobotany and Zoopharmacognosy (IEZ) was founded by two biologists in 1995 as a means to attract scientific attention to the subjects of
- traditional herb use for both people and animals (ethnobotany; ethnoveterinary) in the NL
- zoopharmacognosy, i.e. the study of the process by which animals self-medicate and promote their health by selecting and using plants, soils and insects to treat and prevent disease.
The reason for creating IEZ as a private knowledge center was a total absence of interest in these (research) topics in Universities in the NL. IEZ attempted to raise funds for research in zoopharmacognosy on many occasions, succeeding only on rare occasions. However students from several (professional) universities often expressed an interest in this subject. Thanks to the work of many students, some knowledge about this subject was gained over the years.
As a biologist, specialized in the study of the history of biology, I recovered some interesting zoopharmacognostical observations in classic herbals and Renaissance books.
For example Dioscorides (circa 50 AD) mentions that the chamois (mountain goat) eats from *Dictamnus* (burning bush) herb when wounded by an arrow and this make the remnants go out of the body. Plinius (circa 70 AD) gives many examples from animal observations, leading to herb or general medicinal knowledge. For example the scorpion can be poisoned by touching *Aconitum*, it cures itself from that by eating *Helleborus*. Swallows use the yellow milk from *Chelidonium* to open the eyes of their young. Ibis birds take lavements when constipated using their beaks, bears eat ants eggs when sick, etc.
These observations were cited a.o. in the Netherlands by Jacob van Maerlant in the 13th century and Jacob Cats in the 17th century. In the Renaissance era the subject was also mentioned in the first printed herbals like Brunfels (1532) and also by Giambattista della Porta (1558), an advocate of the doctrine of signatures (ws 2A). After 1700 this topic received no more scientific attention until a publication of Wrangham, Huffman and Goodall in the 1990-ties mentioned chimp-self medication in the Gombe national park in Tanzania. But still there are only a few scientists working (worldwide) on this complicated topic.

Studies by IEZ
Students from several private schools for animal naturopathy as well as students from professional agricultural universities performed several studies on primates, horses, goats and cattle, supervised by IEZ.
The methodology used was mainly focal animal sampling (FAS); taking score of the number of bites (primates) or of the number of seconds spent on grazing specific herbs (goats and cattle). Statistics were in some cases purely descriptive and on other occasions hypotheses were tested with students t-test or Anova (SPSS).
Preliminary studies always involved
- *ad libitum* sampling observation studies to explore the study area and to allow the animals to get used to the observers;
- scan sampling to estimate quantitatively the different types of behavior;
- a global or detailed inventory of the local vegetation;

- imitating the animals foraging behavior to estimate the bite size;
- assessing health condition and/or temperament of the animals in the study.

The studies in chronological:

*1. Studies on woolly monkeys (*Lagothrix lagothricha*)*
During 1996-1999 several observational behaviour studies were performed in the Apenheul primate zoo (NL) by the two IEZ biologists (Tedje van Asseldonk & Arend de Haas) , training students and a biologist from east Europe in general research methodology [1].
In the woolly monkeys (*Lagothrix lagothricha*) area we identified 123 different plant species (some could not be specified beyond genus level) belonging to 53 plant families. In order to quantify and compare this to the consumption, of all plants present the number of bites that were available for eating was estimated. To estimate the size of a bite three observers imitated the monkeys foraging behavior, carrying out 10x10 samples for each vegetation type. A bite of an herb was estimated to be 2,3 (+/- 0,8) gram; a tree or shrub leaf bite was smaller; a bite of grass was 3,9 (+/-1,8) gram. The total amount of available bites present for *Lagothrix lagothricha* in the enclosure was estimated to be 25,215,468 bites (6090 kg). As this was an early season (June) inventory it is likely that later in summer more bites were available.

In 1996 we reported for the woolly monkeys (*Lagothrix lagothricha*) the consumption of 43 different plant species from the wild; in 1997 the number of species was 44. Large differences in plant choice between individuals and between specific days were found. The average plant consumption in both years was about 7g per animal/hour (22 bites/hour); additionally 4-6 insects/hour and 2 bites of sand, pebbles or clay were consumed averagely every hour. Both years, about 25% of the plant consumption was found to be of the Fagaceae family. Two plants (trees) in this family were *Quercus rubra* (oak) and *Fagus sylvatica* (beech); they were abundantly and equally available. Yet the consumption of *Quercus* was 3 fold (in 1997) to 10 fold (in 1996) that of *Fagus*. There was also a substantial consumption of *Berberis* spp (10-15%). The preference in the consumption of trees and shrubs appeared to be rather consistent amongst the group members. There was more animal specificity in the choice of herbs. Summarizing specific herb preference was reported for plants of the Asteraceae, Caryophyllaceae, Rosaceae, Boraginaceae and Urticaceae families; plants that are are also well known medicinal herbs in the herbal tradition in the NL. This tradition will be illustrated in workshop 2B.
It may not seem very much if an animal eats 2 or 3 bites of a herb. But the dosage of these incidental bites is approximately proportional to the human dosage when using these herbs as a food supplement or a home remedy. 2 bites = 5 g/day (fresh) is about 0,5 g/dry = +/- half of human daily dosage for many herbs.
Amongst others we registered the consumption of: *Taraxacum officinale, Matricaria chamomilla, Urtica* spp*, Plantago* spp*, Impatiens parviflora, Rumex spp, Aegopodium podagraria, Glechoma hederacea, Trifolium spp, Fragaria vesca, Myosotis arvensis, Stellaria media* and *Polygonum* spp*.* In 1998 there was a change in the housing of the woolly monkeys and in 1999 the studies with these primates had to be discontinued.

2. Studies on other monkeys (mainly squirrel monkeys, Saimiri bolivienses*),*
These studies were performed both in Apenheul (NL) and in Vallee des Singes (Fr) during 2000-2003. The enclosures of the squirrel monkeys (*Saimiri boliviensis*) were not quantified for vegetation, as was the case with the woolly monkeys. The plots were rather new and the list of plants present was available in Apenheul. Over 97 different species were planted, and in the area's that were used for observation the presence of 46 species was noted. The fact that these monkeys were small and quick created a problem. The focal animal sampling method could not be used and a new observation method called location sampling was developed.

In Apenheul Zoo the consumption was registered of 17 (in 2000); 19 (in 2001) and 16 (in 2002) different plant species.
As with woolly monkeys, a great deal of the foraging behavior consisted of catching of insects: about 8 % (2000); 10 % (2001) and 12 % (2002) of the total amount of bites. These monkeys have a preference for grass, flowers and flower- and leaf buds (*Rosa* spp, *Silene dioica*) and nuts and other parts of *Fagus sylvatica*. About 10 bites an hour were recorded, thus we concluded that the spontaneous foraging activity is a substantial part of their daily routine and probably also for this species an important possibility to perform stress-reducing behavioral choices [2]. Other primate species were studied incidentally with comparable results.

3. Studies on horses and cattle in nature reserves
4. Study on goats regarding grazing behavior on an organic farm
5. Studies on cattle in organic farms
These studies, performed in 2003-2006, 2008, respectively 2010-2012, will be presented in the workshop 1.B.

Studies by other researchers
* Mike Huffman [6] has been very active in the field of primate zoopharmacognosy research. He described bitter pith chewing with *Vernonia amygdatina* and whole leaf swallowing with *Aspilia* spp. Once a chimp was seen obviously with belly pain, she dragged herself to this *Vernonia* plant and ate the bitter tasting stem piths. Next day she seemed cured. Pharmacognosists found indeed bioactive substances in this plant. Later Huffmann described a relation with local ethnobotanical knowledge of this plant. In the *Aspilia* example, a plant that seems to be eaten a lot by chimps in the rainy season (when worm pressure is high) pharmacognosists also searched for medicinal compounds, but closer observation revealed that the hairy leaves were fold and swallowed as a whole, they left the body undigested! So this is very interesting as it points to a physical, not a chemical, vermifugum! Another important thing that we discussed with him when he was on a working visit in the Netherlands, was that we both would try to establish a relation with health conditions other than acute illness. He also co-published about differences in foraging patterns of pregnant and non-pregnant monkeys.
* Michaelle Sauther did a study on lemurs in Madagascar. She noticed differences in leaf and fruit consumption between males and pregnant females. Not easy to explain them [7].
* Another (more recent) example is the study of Carrai et al. These researchers have addressed the foraging behavior in the field, took samples of the several meals and made chemical analyses (in a laboratory) targeting specific compounds of the plants. In this case the percentage of condensed tannins was analyzed, both in the vegetation present and in the food used. Here also there are remarkable differences that cannot be easily explained. My suggestion for an explanation was that maybe the tannin content in itself is not so important, but that this content might be related to the flavonoid content of the plants, and that content could be related to effects on the estrogen receptor and that might explain the increased consumption around the labor period [8]. Just a hypothesis though!
* Very interesting studies by Sabine Krief and colleagues showed how the consumption of some plant species together with specific earth (geophagy) provided good anti parasitic activity, not as such but in combination after digestion. HPLC analyses showed clearly differences in compounds that were absorbed when digestion took place with our without this specific earth (clay) present. This should make us modest, as we humans appear to be not the only species that created a pharmacopoeia with complex recipes [9, 10].
* There have been many examples in literature and there is an increasing amount of publications about non-primate animals using herbs in many ways. Birds and ants provide anti-parasite treatments to their nests by including aromatic plants. Since Cindy Engel has brought several case reports together in her book [11] and there have been numerous new reports. People phone to the IEZ all the time telling stories about how their dog digs up specific roots to chew on them; how their horses during a ride suddenly stop and go to eat a

certain plant when they spot it; how cats drink herbal teas quicker than their owner gets at it (this is not even rare; just google on it and you will see lot of examples!). We are only beginning to understand the complex interactions between the animal and vegetal world. Just one recent publication (not ours) I will mention here: the consumption of a progesterone effective *Vitex* spp apparently reduced the fertility of female baboons during the rainy season [12].

Discussion

Animals appear to have a partially innate and partially cultural (learned) capacity to select healthy food plants cq medicinal herbs, both in their natural environment and in captivity. What may be the implications for the way that we take care of the animals that we keep in captivity?

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1. B. Herbs in pastures and the health of grazing cows and goats (2)
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Abstract
Recently IEZ has conducted studies into the grazing behavior of dairy herds, with a focus on medicinal herbs, both in the situation of free ranging in nature reserves as in organic farms. This research was performed in cooperation with other research institutes in the Netherlands. Methodology and results (interesting and promising) are still under discussion. Input on possible designs for follow-up studies is welcome.

Introduction
IEZ started in 1996 with zoopharmacognosy research in primate enclosures. We generated many data, which we compiled with some basic (summary) statistics; hypotheses were not yet tested. One of the things we noticed was that great differences exist between the individual animals in their specific consumption; it appeared that dominant animals had more herb knowledge. We also had the impression (we could not prove this statistically though) that on warm days, when there was a lot of herb consumption (because the animals went outside), the majority of this consumption was from plants and plant compounds, which traditionally belong to the domain "cold" (this concerns plants with mucilaginous compounds, silicium and/or tannins as their main active ingredients; a further explanation of this terminology will be given in workshop 2B). This may have to do with the fact that the majority of plants available were of a "cold" nature. When the weather was cold, we saw less spontaneous plant consumption (because the animals liked to stay inside) but the consumption had a relatively larger amount of "hot" plants (i.e., referring again to workshop 2B, plants with volatile oils and bitters as main active ingredients). This gave us a clue about a possible way to link health conditions to plant consumption in a way that could be evaluated statistically and by doing so to overcome the "anecdotal" character of zoopharmacognosy.

Studies on horses and cattle in nature reserves
As the study setting in the primate zoo Apenheul changed too much, and also to give IEZ research a more practical output to husbandry, our research topic changed to herbs used by cattle [1]. By doing so the work of Utah professor Provenza was very inspiring to us [2]. He published interesting studies for example about detoxifying plant combinations for grazing animals and about sheep preferring tannin rich foods when they have worm infection.

In several nature reserves in the Netherlands fee ranging cattle and horses are new phenomena since the 90's. They offer an interesting study opportunity, not only for IEZ [3 -> 1A]. The scarce nature reserves in the Netherlands are densely visited, and the animals are accustomed to people observing them. IEZ supervised several students in the reserves in the years 2003-2006. Two colleague biologists cq naturopathy students were interested in the subject and observed cattle and horses in several nature reserves, noting a great biodiversity in their meals. However a relation between health problems and consumption of specific herbs could not be established. There was the difficulty that the animals were not under veterinary control all of the time and also the time-consuming observations had to be done with just a few people, that left out the possibility of regular health checking observations. On one occasion Rienk Noordhuis tried to sample faeces and test them for worms but these studies could not be completed [4 -> 1A]. In 2005 IEZ was approached by three students of the agricultural professional university in Den Bosch. For several months they observed a herd of cows in the nature reserve 'Millingerwaard' (close to IEZ), noting their grass and herb consumption. Interestingly, the cows that were pregnant consumed a larger percentage of herbs (= dicotyle plants) than monocotyle plants (grass and related species); compared to the non-pregnant cows; a significant ($p < 0,05$) difference. Actually we had expected just the opposite: pregnant cows would avoid herbs for the toxic compounds

such as phyto-estrogens. As the herds were free ranging and there were bulls around too, the non-pregnant cows were also the younger cows. In this study we also focused on plants with (potential) hormonal activity, but as every cow has a more than specific grazing pattern, we could not find group differences in relation to specific plants with a statistical significance. It appeared that *Urtica* spp (nettles), *Cirsium arvense* (cursed or creeping thistle), *Trifolium repens* (white clover) and *Taraxacum officinale* (dandelion) were the most commonly consumed plants by the pregnant Galloways. The pregnant Galloways were also observed to consume more composites than other dicotyle plant families compared to non pregnant cows [5 -> 1A].

After the 2006 IEZ study with cattle in a nature reserve, that had as a result that pregnant cows ate (in percentage) more herbs than non-pregnant (younger) cows, we decided to look further into the relation between individual herb consumption and the constitutional and/or conditional situation of individual animals.

Grazing behavior of goats on an organic farm

In 2008 two students from the professional agricultural university Dronten further explored the idea that resulted from our primate studies: that animals were in fact balancing their health by their food choice. The possible relationship between constitutional humoral temperaments and plant consumption were observed. The four temperaments were defined using the traditional European naturopathic system based on Hippocrates; IEZ had designed a graph and a question list for this. The study included 16 goats: four goats per temperament; these were picked out by the farmer. It was interesting that after a brief explaining the goat farmer immediately understood what four temperaments in extrema would look like and she pointed them out without hesitation. Then they were marked with paint in four colors. As classical herbalism defines herbs in wet, dry, hot and cold; the farmer also picked out wet, dry, hot and cold goats for this study. Wet goats are flexible, peaceful, group animals and more directed to the environment. On the other hand, dry goats are braver, solitary minded, stubborn and more independent. Hot goats are dominant and active, cold goats are of a slower, non dominant type. All goats were observed in three observation blocks for 1 hour and 10 minutes each. The results confirmed some of the expectations. Wet goats tended to eat more clover than the dry goats, on average 50.42 seconds versus 13.17 ($p = 0,148$). Clover is a dry and a warm herb which may be the reason why a wet goat chooses it. There was also a difference in the grass consumption, this exclusively concerned the lower part of the grass. The dry goats tended to eat more of the lower parts of the grass than the wet goats (difference 91 versus 52 seconds/hour; $p = 0,075$). The lower part of grass is more wet and warm than the upper part, this could also be a reason why a dry goat chooses this plant.

Hot goats tended to eat more grass (*Poa* spp) (80%) in relation to dicotyle plants; cold goats ate circa 70 % grass. The cold goats took less of the upper parts and more of the lower parts of the grass. The hot goats ate more of the upper part of the grass, the difference had a $p < 0,05$.

The cold goats tended to eat more dandelions ($p = 0,14$). The study was small, but the results looked promising.

Confusing factor in this study was the fact that both hot and dry goats seemed to be rather dominant animals and the dominant goats ate more of the alfafa that was fed in the morning before the goats go outside. Could it be that the non-dominant goats compensated this by eating more clover in the field?

One obvious fact that the students noted was that every morning, when the goats were taken to a new grass field, the herbs were eaten first, and the grass (*Poa* spp) later. This was an eye opener for the farmer too. Attention should be given to the choice of a greater variety in plants on the farm for the well being of goats [3].

The study was criticized by other scientists because of the use of a non-validated temperament score. Therefore the next study had a different design.

Grazing cows on several organic farms

The 2008 goat study had left the impression that there was a difference between dominant and non-dominant animals related to their herb choice. The next step would be a study on cows on several farms, that would check for these differences. This study was done by two students of the agricultural professional university Den Bosch.

At the same time there was an ongoing study for a master thesis in organic agriculture by Sibilla Laldi, an Italian herb expert. This was part of an ongoing government funded project of the Louis Bolk Institute (LBI, a private research center for organic agriculture and complementary medicine in the NL) [4]. We cooperated intensively in these both studies.

The Laldi study was initiated when several farmers observed that their cows seemed healthier when they grazed on pastures rich in herbs. They felt that there might be a link between a diverse diet, with more than just grasses, and the cow's better performances. The project was set up to investigate this claim applying a scientific method that could measure if cows eating more herbs were really healthier than others, and this appeared indeed to be the case.

I will present you the Laldi and the IEZ study, and another LBI project in which we cooperated, and discuss with you possible follow ups.

Materials and methods of the 2011-2012 study

Twenty-two enthusiastic dairy farmers throughout the Netherlands took part in the Laldi MSc study which lasted one year, between spring 2011 and spring 2012. The study measured, amongst others, the grasslands botanical composition, both in number of species and their meaning for cows' health, and the health of the cows themselves.

Out of these 22 four farms (with a high number of medicinal plants in their pasture) were selected where the IEZ students would do focal animal observations, linking the individual herb choice of the cows to a health condition (focus on pregnancy) and temperament (focus on dominant/subordinate).

To identify the difference between an interesting pasture and a non-interesting one, the definition "Medicinal Herb Enriched grassland" (MHE) was introduced and the level of MHE was measured for each of the grasslands of the participants group.

First of all, an analysis of the composition of the grasslands was done by visually sampling the vegetation. For each farm, a series of 100 samples was taken twice, once in spring and once in summer, to identify which species were present. The method used is called "dry weight ranking" because it works by assigning a rank (1st, 2nd or 3rd) to the plants contained in the sample quadrant (50cmx50cm), according to their estimate dry weight. This method takes a well trained eye to be effective, but once the surveyor has trained enough, it has proven to be a very reliable method, and much less time consuming than cutting and drying samples of vegetation. In the end, the sum of contribution of each species is calculated in percentage and defined as "dry weight percentage of species X of the total" (DW%). As the sampling was done in two different seasons to better capture all the range of species present, the DW% of each season was summed up and the final result is the average of the two.

After knowing the composition of the grasslands in dry weight percentage, a weighting factor was applied. This means that those species which are known to have a potential beneficial effect on cows' health were assigned a +1, the poisonous species a -1, and all the other species, mostly grasses, non-interesting in terms of medicinal value, were given a 0. Multiplying this numbers by the amounts measured for a given species gives a value which was called "MHE grasslands value".

A comparison was made to see if different farming type (conventional, organic or biodynamic) were also different in terms of Medicinal Herb Enriched grasslands values. The results showed that this difference existed between conventional and organic ($p<0.01$) and conventional and biodynamic ($p<0.05$), but organic and biodynamic farms were similar. The average value of MHE grassland for conventional farms was 20.2 points, with lowest value being 10.3 and the highest 34.8. Organic farms scored on average 40.0 points, ranging from 21.3 and 62.4, and biodynamic farms had on average 33.4 points, with values comprised

between 21.4 and 46.7.

The fieldwork by IEZ students was performed from the 29th of August until the 21st of October 2011. On four different dairy farms, sixteen cows (4 in each group on each farm: pregnant, non pregnant, dominant, subordinate) were observed, each 10 times in a period of 30 minutes per cow. For the observations the focal animal sampling method was used. An inventory of the herbs in the pasture was done by using the Braun Blanquette method. Also, a list for the health score was used to get a better understanding of the cows health. Dominance was assessed by studying behavior of the herd with the time sampling method. The dominance assessed this way was fully consistent with the dominance patterns known by the farmer [4]

Results

The Laldi study found a significant inverse correlation between the Medicinal Herb Enriched value of pastures (MHE) and the average number of daily doses of antibiotics per animal per year (ADD). This means that, in this sample of farms, the higher the value of MHE calculated for the grasslands, the lower the amount of antibiotics used. Even though many factors can contribute to create the environment for low or high antibiotic use, it was interesting to notice that the quality of pastures seems strongly correlated with the antibiotics outcome. Other interesting correlations were found, for example between the amount of concentrates fed per cow and the secretions from nose and eyes, sometimes a symptom of BRD (bovine respiratory disease), and between concentrates use and dirtiness of the cows' coats, which could be explained as a result of an overall lower fiber ratio in the diet, possibly leading to more diarrhea. Concentrates were also correlated with higher milk yields, and milk yields were instead inversely correlated with MHE values of pastures, suggesting that those farms where production is less intense are also richer in pasture diversity.

The IEZ/HAS students had a very small sample size to obtain significant differences between study groups. The study concluded that there was no significant difference in the total grazing time on herbs between pregnant and non pregnant dairy cows. There was also no significant difference between pregnant and non pregnant dairy cows in the grazing time on the specific herbs, such as dandelion, clover, and buttercup per farm. However, during this study it was again observed that cows graze selectively on certain herbs. Each cow has its own temperament and diet, but this does not seem to be related to pregnancy. On farms with a large variety of herbs the cows had a better health score. It can not be said with certainty whether herbs actually affect health and which other management factors play an additional role on the health of dairy cows. As a trend it was registered that grass consumption in the morning was less than in the afternoon and there was a significant difference in herbal use between the morning and afternoon. Cows eat more herbs in the morning than in the afternoon ($p = 0.000$). The t-test and ANOVA Analysis of variance showed that temperament also had no significant effect on the total herb consumption ($p = 0.702$). But it appeared that subordinate cows ate more grass in comparison to dominant cows ($p = 0.034$). The consumption of specific herbs was too incidental to be tested.

Trees as a fodder for farm animals

There are several advantages for herbs in the grass: increased biodiversity, more resilient vegetation (the BBC documentary: A farm for the future by Rebecca Hosking shows how this works), better mineral and vitamin providing fodder.

A growing number of farmers in the Netherlands is getting interested in planting more trees around or in their pastures (silvopastoral); also in bigger amounts (agroforestry). Apart from increasing the biodiversity on the farm by doing this, they think about using branches and leaves as fodder. For example willow (*Salix* spp) branches are fed everywhere in zoos to nearly all animals (also to primates in Apenheul) and all animals seem to like this very much; in particular goats [6].

The farmers group asked IEZ for an opinion on the medicinal aspects; we made an overview for them, using different colours to group the trees with different types of secondary plant compounds (such as: saponins, tannins, mucilaginous compounds, volatile oils) that may help them increase not only biological (species) but also chemical (medical) diversity for the animals. In this respect a diversity of bioactive compounds can be offered to improve possibilities for self-medication by the herds [7].

Discussion

The results of the Laldi study confirm the link between herbs and healthier cows and it offers a new perspective in the strategies to achieve lower antibiotic use on farm, both to contrast antibiotic resistance and reduce veterinary bills. Furthermore, growing herbs on grasslands could optimize the productivity of low-fertility areas, as herbs, in general, do not require high level of nutrients and thrive in sub-optimal soils.

The IEZ study did not result in significant confirmation of the early findings. However, the extra consumption of herbs in the morning is likely to indicate that the availability of herbs is less than what would be desirable. As in the previous goat study, students again observed that the animals preferred herbs and ate them before starting to eat grass.

Experiences of farmers with leaves and branches of tree (esp willow trees) as fodder are positive. An increase in biodiversity is also an increase in possibilities for self-medication.

No research has yet been done into the ways animals use this variety when offered.

How can we make these lines of research of interest for capable researchers that have access to fundings for their work? What is a methodologically sound way to move forward and get results?

Acknowledgements

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6. Website of this farmers group: www.voederbomen.nl; it also contains a film that shows how young willow trees are harvested and how goats like to eat this.

7. This IEZ advice is available on http://www.voederbomen.nl/wordpress/wp-content/uploads/2012/04/Medicinale-en-etnobotanische-aspecten-van-potenti%C3%ABle-voederbomen-voor-melkvee.pdf

2. A. The doctrine of signatures (DOS) in history and in modern herbalism

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Abstract

The discussion whether form follows function or form creates function is closely related to the question of an existence of any (divine?) architecture in the (evolution of the) living world and therefore a no-go-area for many modern scientists. But could there be a mutual interaction (morphogenetic resonance) as suggested by the biologist Rupert Sheldrake? How does astrology fit in here? And does this learn us something about how animals in the wild gather food and drugs; may this be compared to the way our ancestors did find their way to medicinal plants?

Introduction

Every culture in the world uses and has used herbs for better health of man and animals. Striking similarities can be found between cultures that differ in time and space. For example *Salix* spp have in many countries been used for thousands of years against fever and pain; and recently there was a study published by the Reading and London universities that showed that totally different cultures as in South Africa, Nepal and New Zealand have in their pharmacopoeias not randomly selected plants, but plants with 80-90% phylogenic relationship [1]. Nowadays this relationship is defined by DNA similarity, but until recent there was only plant morphology as a tool to group plant families. This was not so bad at all, given the stability of the old groupings of plants in modern days. If we accept the fact that family related = DNA related = secondary compounds related, the basic idea that the morphology of a plant can have some relation to its medicinal properties is not totally unacceptable.

The philosophy that human cultures construct to explain the (obvious) effect that herbs have on humans and animals can be very different, both in history or in cultures. Magical concepts were never put totally aside in rationalist societies but often went underground to turn up again in later ages. The traditional knowledge of the "powers" of herbs came first, while the conceptual framework for their explanation (be it the doctrine of humors, of signatures or phytochemical) was developed later.
This lecture will address the question in what light the philosophical exercise that is called 'doctrine of signatures' can be seen. We will take a recent publication of professor Bennett as our starting point [2].

Just a little donkeys bridge?

In the Netherlands we have the word *ezelsbruggetje* (little donkeys bridge; from the old greek: pons asinorum) for a mnemonic aid: something that will help you remember things that are difficult to learn by heart. For example, the first 15 digits of the mathematical constant pi (3.14159265358979) can be encoded as "Now I need a drink, alcoholic of course, after the heavy lectures involving quantum mechanics"; "Now", having 3 letters, represents the first number, 3; I is the second number, 1, etcetera.
Bennett states that the doctrine of signatures has this function [2] and of course he is right. Out of many plants that were known to promote bile flow, it is not unlikely that the ones with yellow flowers survived the ages of cultural (r)evolution better because the color fits the use of the plant. Same goes for red in relation to blood, white in relation to phlegm, etc.
But is this the only useful aspect of this philosophy? That is rather unbelievable for a philosophy that has been around for so long. So could there be more to it?

The DOS (Doctrine of Signatures) in old herbals

Lithospermum was already mentioned by Dioscorides (ca 50 AD) for her properties of stone dissolving (kidney and bile). The name *Lithospermum* means: seed that looks like stones. But Dioscorides does not refer to this likeliness; on other places he warns against these type of interpretations. Plinius (ca 70) writes on *Lithospermum*: "The pearls (seeds) are as beautiful as the best craft work. You only have to look at the plant for a moment to recognize

it as a remedy against kidney stones." The same goes for the red tincture cq oil derived from *Potentillla erecta* and *Hypericum perforatum,* two traditional wound remedies. So the old "experts" do not agree on this point.

To discredit the "Doctrine of Signatures", the focus of attention is usually on these simple examples of medicinal effects related to the external appearance. Remarks in this sense can be found in nearly all classic herbals, from Plinius up to the Renaissance, but you find them along with warnings against such a superficial interpretation. This makes one curious as to what deeper interpretation could be possible.

It is notable that regarding this subject authors were often unable to clearly put into words what was meant.
Dodoens for example, the most well-known Flemish/Dutch authority on medicinal plants of the 16th and 17th century, gives an explanation for how the medicinal effect of a plant arises. He states: other than food plants, the medicinal plants alter or overwhelm the body with for example heat. To become effective in this way the plant parts must be altered by preparation and by digestion in the body. He describes four kinds of plant powers, the first three being related to physiology and taste, and the fourth is only described vaguely. The first plant powers are the ones that are warm, cool, moisten or dry or combine two of these effects. The secondary powers follow from these: emollient, pus-creating, indurant (hardening), diaphoretic, condensating (fattening), opening, constringent, astringent, detergent, expurgent (cleaning, thriving), narcotic, rubefacient (irritant) etcetera. However, Dodoens does not explain how these secondary powers arise from the first. The third kind of powers, that stem from both the first and second, are the properties for maturing, wound healing or bone healing, and also diuretic, litholythic (stone-solving), emmenagogeous, abortive, lactagogeous (milk enhancing), sperm-enhancing and cough removing properties. Apart from that Dodoens mentions a fourth kind of power, which is not derived from any of the forces mentioned before, but is derived from experience and immaterial powers like magnetism and signs given by the external appearance. Animal poison, and theriacs and amulets that can cure it, are some of the examples he gives.
Although Dodoens seems to make a clear reference to the doctrine of signatures here, as a means of recognizing the medicinal properties of a herb, in several other places in the book he warns against this doctrine, that has given rise to many fatal mistakes. Not only he, but also Dioscorides (ca 50), Plinius (ca 70) and the Renaissance writers Brunfels and Fuchs do so.

Immaterial concepts related to pharmacology can be found more explicit in the teachings of Paracelsus (16th century). Whenever he is looking for the quintessence (quinta essentia) of remedies, he has much in common with the later Hahnemann, founder of homeopathy. This was analysed in detail in the PhD study of a Dutch physician, Oosterhuis in 1937 [3]. Both Paracelsus and Hahnemann moved away from the chemical (toxical) aspects of medicinal herbs and explored and used their invisible "energy". But by Hahneman's time (around 1800) the opposite route had already been taken in main stream medicine, that valued the most drastic medication the most, notwithstanding the toxicological risks involved [4]
Reading Paracelsus' works about the reciprocal influence of macrocosmos and microcosmos uncovers some aspects that are quite similar to thoughts of Hahnemann (circa 1800) and (contemporary) Rupert Sheldrake.

Related external and internal plant properties
Plants have evolutionary adapted to all kinds of (hostile) environments by making chemical and structural adaptations. To prevent themselves from being eaten they synthesize certain chemical compounds, most of them are called secondary plant compounds. They are deemed responsible for the medicinal effects of herbs, but also for some external marks, such as colors and smells. Apart from that, plants show other strategies, both to defend themselves against grazing or to be better adapted to non-biotic factors (such as heat,

inundation etc). Most of these adaptations show themselves in typical plant structures, such as leaf devision, thick leaves, hollow stems, etc. Therefore both the chemical and structural adaptations are of interest for the doctrine of signatures.

It is not a coincidence that Moerman [5] found, as I confirmed for the Netherlands [6] that regarding the relative importance of plant families for medicinal use on the northern hemisphere the families of *Apiaceae*, *Lamiaceae* and *Asteraceae* are relatively over represented. These families house a lot of aromatic (fragrant) plants. We know now that a lot of fragrant plants have antibiotic as well as digestive, expectorant and diuretic properties.

Take as another example plant compounds like silicium, saponin, and tannin: they can not be smelled, but the qualities can be felt or seen and so they were included in the knowledge system.

Looking at the exterior of a plant to tell something about its medicinal value is often considered ridiculous. But chemotaxonomy tells us that an evolutionary relationship, that is visible by typical visual characteristics of a plant family, is often an important clue for specific secondary compounds. If you recognize a *Rosaceae* plant, you will probably do this by the saw edged leaves, and you are quite sure to have a plant at your hand that is not poisonous and will have lots of tannins so it can stop diarrhea or close a wound. A non-educated person may turn it around and see the saw-edge as a sign for a plant to be used on wounds. Now this example is invented by myself, I never saw it in any old or modern book , yet it makes a lot of sense. Is it just a mnemonic aid? If you read anthroposofically orientated botanists, you will find they often have inspiring remarks noticing unexpected correlations between for example specific leave forms and medicinal properties of plants [7].
Why is a herb with a hollow stem supposedly good for people with respiratory problems? Maybe ecology can give an answer. Could it be it is not because the hollow stem looks like the trachea, but because the hollow stem is the plants evolutionary answer to a lack of oxygen in the soil. Maybe some aspects of the physiology that deals with a lack of oxygen can be addressed by some of the chemicals in these plants?

It is only ridiculous to think that red plants have a positive influence on blood, and yellow plants on bile, if you are not prepared to let experience in medical practice be your **major** guide. Unfortunately that is what some people (also some anthroposophical physicians) seem to do, and that is a practice I cannot agree with.

Discussion
Theoretical concepts on plant activity evolve along with human knowledge. They shouldn't contradict the well documented activity, the known chemical contents, or other scientific findings, but must at all times consider, include and complement these findings. But the strictly chemical approach of plant activity that is very popular nowadays could be more modest and admit that as yet undiscovered non-chemical forces of plants may also play a role in traditional herbalism.

The focus on the possibility to combat diseases with the strongest (often very toxic) herbs available has left many interesting observations and valuable experiences of classic herbalism unused. The individualized prescription of herbs, taking into account not so much the disease combat, but also (or mainly) the possible health benefits related to specific patient-characteristics, is nowadays still in use by naturopaths and practitioners in Ayurveda and Chinese herbalism. Only a few studies have been done to evaluate the efficacy of this kind of patient-specific prescriptions, be it in Eastern or Western traditional health care. When talking to these practitioners they often admit there is an intuitive aspect in these individual prescriptions that they find it hard to talk about. We cannot rule out that "non-material aspects" were and are a part of the herbalism practice.

Some of the (previously orally transferred) craftsmanship concerning the (folk) knowledge on herbs possibly never entered a printing press. The persecution and murdering of witches, that had a lot of herbal knowledge, in 15th/16th century makes it even harder to recover this practice.

Throughout history people have tried to embed health problems in spiritual aspects of their culture. Religion and astrology foresee both in a need for spirituality because they both offer a connection with the transcendent forces; be it a God (religion) that is present everywhere, or be it a cosmic connection, offered by an astrological concept of the universe.
Also the doctrine of humors offered this connection; this may explain its popularity over the ages (from the last centuries BC until 1700 AD). This doctrine however was put aside rather rigorously at the end of the 17th century because in that age human anatomy and physiology research brought to light some mistakes in the Hippocratic and Galenic aphorisms. In folk medicine the astrological world view and doctrine of signatures may have compensated for this spiritual loss in (science orientated) medicine, and they still do. Currently the number of web sites that Google gives for doctrine of signatures is 1.750.000 and herb astrology gives 3.640.000 hits, in spite of the ongoing rationalism of phytotherapy as a science.

Could it be, that what Paracelsus, della Porte, Boehme and Culpeper attempted to do was to make a synthesis of all experience- and knowledge of their age concerning particular plants? That they wanted to put it into a concept that was broad (holistic), and used the only language they knew for that, the astrology? My hypothesis is, that in an era that had no possibility to do chemical analyses on plants, the smell, taste and exterior looks of plants often gave important clues for their physiological effects (as will be discussed in workshop 2B); but also that the doctrine of signatures was used to explain some of the transcendent effects comparable to what our culture did with the evolution theory in the 20th, and with system biology in the 21st century.

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2. B. Traditional concepts of European herbalism related to chemical ecology

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Abstract

Traditional European herbalism has two major therapeutic principles: a constitutional (holistic) therapy and a patient specific approach. The basic concept is often referred to as the doctrine of four humors. The available medication (mostly food and herbs) was analogously allocated to four categories: hot or cold and, in addition, wet or dry. Currently these concepts are still in use in naturopathy practice. Based on a literature study IEZ presented the hypothesis that this classification of herbs may be related to the function of the secondary plant compounds for plant defense as described in chemo-taxonomy and chemical ecology.

Introduction

In the Netherlands, as in several other European countries, naturopathy draws on the works of Hippocrates. These works were in fact not written by one person but by a group of physicians in the period around 500-300 BC. The 58 works have in common a rational and empirical approach towards sickness and healing. The two major therapeutic principles that are outlined in the *Corpus Hippocraticum* (CH) are a constitutional (holistic) therapy and a patient-specific approach (in time, dosage and 'nature'). The concept is often referred to as the doctrine of humors (**1**). Later, in the time of Galen (129-210 AD [**2**]), the forthstanding medications (food and herbs) were analogously classified as being of a hot or cold and, in the second place, of a wet or dry nature.

Therapeutic plants are, in every age, positioned and elaborated within the different philosophical frameworks constructed around health and disease. The doctrine of humors, which came into existence in Greece more than 2000 years ago, is the example that is illuminated here, but other traditional health systems developed in Asia in about the same period in a comparable way. For example, the Chinese culture has maintained her traditional healing system for a longer period than Europe and can therefore draw on a vast amount of literature. In this literature, the use of medicinal plants is explained analogously to the use of acupuncture needles in terms of balancing the body's energy system. The exact nature of the energy that is involved here has not (yet) been clearly defined in a way that would make it accessible to Western science. Recently, several books written by Chinese herbal practitioners tried to explain the 'energetics' of Western herbs in terms of traditional Chinese philosophy (**3**, **4, 5**, **6**). Of these clinical textbooks, Ross' (**6**) is most thorough as he mentions several classical European herbals. In 2007 Thom Ehrmann, a TCM practitioner and scientist working in the London School of Pharmacy has done a great study showing how TCM herbs and their TCM indications are related to chemical compounds that are present in this herbs (7).

In our work (8,9) we tried to connect traditional and modern Western herbalism. Therefore we attempt to understand the 'nature' of European herbs within the conceptual framework of traditional European medicine.

Starting with the CH, then developed more in detail by Galen and medieval authors following Avicenna, the 'nature' or 'quality' of European herbs was, in the classic herbals, defined according to the basic rules regarding all processes in the universe: as a result of a double polarity of two antagonistic forces or energies (hot/cold and dry/wet). Therefore, the herbs were, like patients, apart from their clinical effects, characterized as being qualitatively related to the four elements and humors. This kind of classification, being part of a cyclic world view, has obvious parallels with the approach of traditional Chinese medicine (TCM), which also draws on cyclic pulsation of energies and the related seasons for patient-specific diagnosis and therapy.

The Concept of Four Elements and Temperaments

Empedocles (490-430 BC) was the first to define four elemental forces that were in his age thought to be at the base of all processes on earth. In his opinion, fire related to warmth, air

to coldness, water to wetness, and earth to dryness. In the CH, this concept was used to describe both man and his surrounding world as a continuously changing mixture of forces, forces resulting from elements that pushed the world in opposite directions. The interaction between these antagonistic forces was thought to bring about an ever-changing reality. The four humors are not elements as in building bricks, but they are a characterization of man's dynamical relationship with the world, relating to the place where he lives, the seasons, his age, etc. Not one humor is pathogenic; but it is possible that an unbalanced mixture is present in man and this can cause disease.

Aside from Empedocles' definition of the elements, the CH characterizes each of the four humors (sanguine, choleric, melancholic, phlegmatic) by *two* basic forces. These are, respectively, wet/hot, hot/dry, dry/cold, and cold/wet. Each combination is analogously represented by the "elemental" forces of air, fire, earth and water. In fact, humors are the elements of nature, visible in man (**1**).
In the doctrine of humors, the world both outside and inside man is analyzed to be a result of certain processes that were described as elements, but they are in fact the anchor points in a circular process, caused by two polarities working in opposite directions.

In several works of the CH, reference is made to the effect of food, herbs and lifestyle on the health of the patient. For example, in *De aere aquis et locis,* it is mentioned that effects of the seasons and winds (hot or cold, wet or dry) are of great importance to the health of a person. More in particular, the work *De natura hominis* (probably not written by Hippocrates but by his son-in-law Pólybus) relates the four seasons to four humors in the human body. For example, a remedy that will expel phlegm by vomiting will have a different effect in each season. In addition, a person who is too hot is advised to visit cold places or eat cold foods. Some general remarks are made about hot and dry remedies that expel the choler (bile), and about cold and wet remedies that expel phlegm by vomiting. In *De alimento,* the effect of food items is said to depend upon specific aspects of the patient, amongst others, the region where he lives.

It was in the period after Aristotle that the scheme of double polarity with organs, gender, etc. was completed. The transformation of elements in the cyclic rhythm of days, seasons, etc. can be better represented in a circular scheme than in a box. Many of these have been drawn, not always in the same way. Because in our day, we are in the habit of placing the north (cold direction) on top of geographical maps, it may be appropriate for a better understanding to maintain this in all figures.
Although in the CH some references are made to medicines (herbs) that have specific influence on the humors, as for example they could dry the phlegm or attract the choler (bile), it was Galen (129-210 AD [**2**]) who made the characterization of herbs most explicit in this respect. He described not only their general influence on the human physiology (wet, cold, etc.) but also the degree to which it was influenced (the stronger, the higher the degree) on a scale from zero to four. Several medieval and Renaissance sources, such as the manuscripts *Tacuinum sanitatis* and *Herbarijs* and the 16th and 17th century herbals of Fuchs, Dodoens, Coles and many others, use the Galenic concepts of the four qualities to characterize or explain the physiological effects of herbs. The allocation is not absolute but rather relational (as will be demonstrated with some examples) and over the ages, critical observers and authors have confirmed several of Galen's classifications and challenged some of them.

In contrast to the CH, the medieval and Renaissance herbals deemed God to be responsible for the analogies that were found between the processes in nature and the processes in man. The *Herbarius zu Teutsch* (1485) states: "Many a time and oft have I contemplated inwardly the wondrous works of the Creator of the universe; how in the beginning He formed the heavens and adorned them with goodly, shining stars, to which He gave power and might to influence everything under heaven. Also how He afterwards formed the four elements: fire,

hot and dry – air, hot and moist – water, cold and moist – earth, dry and cold – and gave to each a nature of his own; and how after this the same great master of Nature made and formed herbs of many sorts and animals of all kind, and last of all Man, the noblest of all created things (…) I considered further how that in everything (…) the four natures of the elements – heat, cold, moistness and dryness – are mingled. It is also to be noted that the four natures in question are also mixed and blended in the human body in a measure and temperament suitable to the life and nature of man."
And the *Grete Herball (1526)* says: "Consyderyinge the cours and nature of the foure elements and qualities where to ye nature of man is inclined, out of the whiche elementes issueth dyvers qualities infyrmytees and diseases in the corporate body of man, but god of his goodnesse that is creatour of all thyngees hath ordeyed for mankynde (…) for the sustentacyon and helthe of his lovynge creature mankynde whiche is onely made egally of the foure elements and qualities of the same (…) virtues in all maner of herbes to cure and heale (…)" (Both quotes from Arbor (10)).

Traditional Definition of the 'Nature' of Foods and Herbs
Galen (129-210 AD [**2**]) made a long-lasting classification of foods and herbs, embedded in the Hippocratic theoretical framework, which was adopted by influential Arab physicians and became the dominant medieval and Renaissance strategy for medicine. From Galen's time until the end of the 17th century, it was common to explain plant activity in terms of hot and cold; both could be absent (in a temperate remedy) or present in the first, second, third or fourth degree. Secondarily, the remedies could have a wet or dry aspect in the first, second or third degree. In the Netherlands, we find this classification in medieval manuscripts and in Renaissance herbals and books about food. Many scientists during and after the period of Enlightenment considered the Galenic classification an irrational way of thinking about herbs, and the classification disappeared from most European herbals after 1700. But in folk medicine, and later also in naturopathy and anthroposophy, this type of classification, and in particular the Hippocratic humors, kept its importance over the ages.

The temperature of herbs in old herbals should not be measured or explained in terms of degrees Celsius. Herb temperature expresses the effect that an herb has on the human physiology. Van Maerlant (ca. 1270 [**11**]) states that everything has the nature of being cold, hot, dry or wet in a certain degree. The first degree means you hardly notice it, the second has a certain influence, the third can hurt your own nature, and the fourth pushes your own nature aside. Culpeper (1652 [**12**]) states that as the primary classification is warm/cold, and both extreme heat and coldness expel any moisture, there is no classification for dry/wet in the fourth degree. Not all authors agree on this but the allocations for dry/wet are seldom to the fourth degree. Culpeper explains the concept of the four elements (qualities) in his essay "The Family Physitian". Hot remedies make offending humors thin, that they may be expelled by perspiration, open pores or bring heat (outward application), warm up the blood, cut tough humors. Cold remedies qualify the heat of stomach, cause digestion, abate fever heat and refresh suffocated spirits, make humors thick, limit choler, repress perspiration. Drying medicines consume humors, stop fluxes, bind and strengthen nature, and stiffen parts. Moist medicines are lenitive and make slippery, make airways less rough, loosen the belly, make the body watery and phlegmatic.

Dodoens (1644 edition [13]) gives a more specific explanation for how the medicinal effect of a plant arises. The primary plant powers are the ones that warm, cool, moisten, or dry, or combine two of these effects. The secondary powers follow from these: emollient, pus-creating, indurating (hardening), diaphoretic, condensating (fattening), opening, constringent, astringent, detergent, expurgating (cleaning, thriving), narcotic, rubefacient (irritant), etcetera. Dodoens does not explain how the secondary powers arise from the first. The tertiary powers that stem from both the first and the second are the properties for maturing, wound healing or bone healing, and also diuretic, litholythic (stone-dissolving), emmenagogeous, abortive, lactagogeous (milk enhancing), sperm-enhancing and cough-removing properties.

The most important way to recognize the powers that plants hold, according to Dodoens, is the smell. Then, certainly under influence of smell, there is the taste. Three of the tastes are warm (sharp, bitter, salt), three are cold (astringent, acid, sharp), and three are temperate (sweet, fat, flat). The sharp plants expel urine, are laxative; the bitters are dry but salt is dryer. The astringent taste makes the tongue rough and dry as it would from unripe fruit. It is not the same as a sharp taste. It can be of a warmer or wetter nature; if wet and warm, it becomes sweet and fat. Fat and glue is cooling and this softens the mouth, as in oil and mallows (*Malva* spp).

In an educational context we often let students try to classify some plants in the old system after tasting and smelling them.
Four organoleptic (by taste, texture and smell) and clearly distinguishable properties of medicinal plants suggest by their opposing principles a relation to the doctrine of humors. These four are:
* aromatic properties (fragrant, warming) – with many recognizable smells, characterized as fire
* mucilaginous compounds (with softening, emollient properties) – giving a slimy sensation when chewed, characterized as water
* tannins (with astringent properties) – recognizable by the drying sensation they provoke in the mouth, characterized as earth
* the bitter principle (with digestive, e.g., salivation-enhancing properties) – a specific taste that, by its effect of promoting saliva, bile, etc., has some characteristics of air.
Bitter plants have contradictory descriptions, also in the old herbals. Because they spread the concentrated ("fire") energy (for example, by increasing the flow of bile), they can be seen as wet or cooling; but compared to mucilaginous or astringent herbs, they are warm because they make things move instead of having a calming and conserving nature. Bitter is normally characterized as warm in old textbooks, but the opinions on allocation of bitter plants like *Taraxacum* differ; they could be called warm by one author, or cold, dry or wet by another. Typical remarks in these discussions are, for example (Fuchs 1543 [**14**]): "It is not a warming herb because it has no bitter or aromatic properties." or, "Gentian is warm and dry, that we can derive from its bitter taste."

When students try to classify plants in the humeral system, in case of rosemary and thyme, they always choose warm and dry. In case of mallow flowers or psyllium seed, they always choose cold and wet. Tannin-rich plant parts like blackberry or silverweed leaves are easily recognized as dry, binding (earth-like). However, in case of bitter herbs like absinthe or dandelion, there is always a lot of discussion about wet or dry. The bitter taste is often characterized as "dry", but as it stimulates salivation, others call it "wet".

In general, most of the authors we studied seem to agree that hot herbs bring about movement, excretion, activity, etc., whereas cold herbs give rest, smoothening or slowing down the digestive (bowel) activity. Examples of extremely hot and dry (fire) plants are garlic and chili pepper, while most of the other kitchen herbs are moderately hot and dry. Extremely cold and dry (earthy) plants are *Papaver somniferum* and *Atropa belladonna*. These are interesting examples because both plants contain parasympatholytic alkaloids and the latter also has very strong proteinase inhibitors and therefore slows down digestion extremely. These herbs were considered witch-herbs and the temperament they promoted, melancholy, was used to explain the behaviour of witches (15). Water-typed plants include salad greens and cucumbers, and air is represented moderately by olives and bread. The most powerful plants, as for example *Papaver, Mandragora* and *Belladonna* that were allocated cold in the fourth degree, were used for the isolation of modern drugs.

In addition to the four types of compounds mentioned that were known to herbalists long before analytical chemistry came into existence, people were aware of the saponin (soap-

like) compounds: the root of *Saponaria* was used for cleaning, as were fruits of *Aesculus* and several other saponin-containing plants. In herbal traditions, “cleaning” herbs are quite often those that have saponin compounds that promote expectoration, faecation and urine flow as a result of irritation of the saliva. In addition, the presence of silicium shows itself, be it in the very hard appearance of the herb (*Equisetum* was used as a casserole brush) or in the hairs (in *Symphytum*, the prickly ash, or in *Urtica*, the nettle). The silicium-containing herbs are used in folk medicine to promote stronger hair, nails and skin in both humans and animals (16).

Material and methods

We compared the allocation of 90 herbs in 12 herbals with the help of a spreadsheet (Excel). Although differences in interpretation of plant ‘nature’ existed, the majority of these plants had been allocated to the same element by different authors. It appeared that Hildegard von Bingen (**17**) and Nicholas Culpeper (1**2**) had rather deviating classifications of herbs: Hildegard because she saw phlegm as the cause of nearly all diseases, and Culpeper who explained the nature and effects of herbs in terms of astrology. This can be traced back again to the four basic elements but obviously this yields additional complications. Coles (18), for example, stated that Culpeper made many mistakes in his book. Thus, only the remaining ten herbals (11, 13, 14, 18, 19, 20, 21, 22, 23, 24) were considered to represent a mainstream group in discussing herb ‘natures’. We started with 90 plants that we tried to allocate according to these herbals. We left out plants that were mentioned in less than five of the herbals. Therefore we ended with 39 plants allocated to hot,cold, wet or dry in the above mentioned ten herbals.

From these ten most congruent herbals, 18 congruent botanicals have been selected; these plants are allocated in a rather similar way by all authors (low standard deviation between author classifications) and each appears in at least five of the 10 herbals. We used these plants to compare the effects in the 'classical' description with what we know nowadays of these effects.

Preliminary results

In line with the Hippocratic principles explained above and confirmed by later authors, the allocation of herbs to an element in a certain degree is not absolute, but it is related to man's condition. It also seems likely that the classification was related to a counterpart considered relevant for the item. An example that can illustrate this is the relative allocation of several grape products.

The *Tacuinum sanitatis* (19) speaks of *grapes* as rather moist and of neutral temperature; this can be represented by the water element. When grapes are pressed to make *juice,* this is a concentrating process, making the product colder and dryer. Then the juice becomes the fermenting *must*: an expanding process that cannot take place in a closed bottle because it will explode. Air is the element here. Again, from must to *wine* is a concentrating (drying) process, taking the product from air to fire; and *aged wine* is considered as even dryer. Eventually when the wine becomes *vinegar*, it loses its ability to raise people’s spirits. The cold and dry earthy realm becomes its domain, and its acidity gives it astringent properties consistent with the centripetal force that characterises ‘earthy’ processes. For the *unripe fruit,* Fuchs (1543 [**14**]) also gives a cold and dry classification to grapes: ripening of fruit is a moistening and warming process. Coles says the temperature of a raisin returns to moderate.

Some other examples can be given: Dodoens (**13**) sees mature olive oil as warmer than fresh olive oil. Grain as a food item is, according to the theory, of a temperate nature when compared to the medicinal herbs, but the classification of *Hordeum vulgaris* (barley) in the *Tacuinum sanitatis* and in all studied herbals of 16th and17th century is rather cold and dry. As for the other main food grains, the authors agree less. For *Triticum aestivum* (wheat), warm and wet is generally accepted (warm but not wet or dry, says Fuchs). A bit colder and dryer is *Secale cereale* (rye), of which Fuchs says, “It is warm and slightly dry.” *Avena sativa* (oat)

is cold as a medicine but as a food, it is warm; the same goes for its drying capacity. Thus quotes Fuchs from Galen.

Congruent botanicals are for example garlic and peppers; they are considered very hot in many cultures. The garlic bulb (*Allium sativum*) is considered hot and dry in the third or fourth degree by nearly all authors. Plantain leaf (*Plantago spp.)* is considered very cool and a little bit dry by many authors. Violets (*Viola* spp.) are mostly considered wet, the temperature classification is less congruent, but mostly cool. Cucumbers are always wet and cool. It should be stressed again that the classification is relative and must not be seen as absolute.

Many post-Galenic authors gave their comments on the Galenic classification, bringing in their own experience with many herbs. Nevertheless, a certain congruency seems to exist, not always on both topics (temperature and moisture) but often on one. The difference between one author's opinion and the older textbooks of his predecessors was often motivated. For example, Hartlieb (1470 [20]) stated violets to be cold and moist, he claims that authors who call them warm are wrong. Fuchs (1543 [**14**]) criticised the Arab physicians and defended Greek medicine. About violets, he says, "many say they are cold, but you must taste them and then you know that they are not." About hops, Fuchs says that authors who consider it cold or temperate are wrong, because it tastes bitter and has a strong smell, so it is hot and dry in the second degree. Tabernaemontanus (1625 [21]) makes the same remark about hops; also, he agrees with Galen on the classification of fennel (warm and dry), but he does not agree (with either) with the degree of the warmth. Dodoens and Culpeper also make their own specific remarks on herbal classifications, correcting, or adding information to, older authors. Nylandt [**22**] mentions several references for each herb, such as the works of Galen, Brunfeldus, Dodonaeus, Fuchs, Duranthus, Mathiolus, Camerarius, Sylvaticus, Fernelius, Januenfis, etc. He noticed the contradictory remarks, for example, that turnips are cold and moist, although some call them hot and dry in the third degree. In the chapter about *Ranunculus ficaria,* he states, Dodonaeus calls it warm and dry, but others call it cold and wet.

Intermezzo: Ecological Explanations for the Presence of Medicinal Plant Compounds
Plants defend themselves with certain chemical compounds, mostly called secondary plant compounds, against consumption by grazers or insects, and against fungi and bacterial infections (25,26). In case of disease or damage, some of the secondary compounds will be synthesised for damage control. For example, synthesis of oligomeric proanthocyanidins with anti-oxidant properties is increased by *Crataegus* spp. in response to drought and cold. There is also more anthraquinone glycoside accumulation in *Cassia podocarpa* in the dry season.

The secondary plant compounds are deemed responsible for the medicinal activity of herbs. The pharmacological effects of these compounds vary, but mostly they are beneficial in a low dose because they can correct small health problems; in a high dose, however, they can be poisonous because they can cause drastic changes. In general, plants can produce a variety of defensive compounds, but in specific plant families, some specialisation has occurred. Plants that concentrate their defence on digestibility reducers like large carbohydrates (in the *Malvaceae*), silicium (in *Equisetum*, in the *Gramineae* family and a few dicotyle families like *Boraginaceae*) and tannins (in the *Fagaceae* and *Rosaceae* family) have a different strategy from plants that invest in specific small toxic compounds like the terpenoids and alkaloids that are found in many dicotyle families of which *Asteraceae, Lamiaceae, Apiaceae* and *Solanaceae* are very typical. At present, much is known about the evolution of the chemical pathways for the synthesis of these compounds (27), but the linkage to the climatic changes and other aspects of environmental pressure that facilitate the chemical specialisations of the plants is far from being sufficiently unravelled.

An example is the rise of the *Gramineae*. When there was a change of climate towards colder and dryer, more severe pressure from grazers benefited plants that had a very low growing point. This is an example of a morphological defence strategy. These plants are relatively unharmed by grazing and need no big energy investment into the production of toxic compounds. Most important food crops belong to the *Gramineae* family.
Many plant species however, rely strongly on chemical defences, thereby using two different strategies (25):
1. Reduced digestibility by large or indigestible compounds: (hemi)cellulose (large carbohydrates), silica (Si), lignins and tannins (large agglomerations of polyphenols) or by proteinase inhibitors. Examples of the latter are found in *Solanaceae* plants.
2. Toxicity, caused by smaller compounds that interfere with physiological functions of the animal: alkaloids, terpenoids, glucosinolates, cyanogens, (steroid) saponins, lectins (protein), toxic amino acids, coumarins, etc. Many of these compounds are specific to certain dicotyle angiosperm plant families. Many of these compounds will activate eliminating processes like urination, perspiration, bile flow, defaecation, etc.

A hypothesis for further studies: is 'herb nature' related to chemical compounds?
In Renaissance herbals the herb monographs are usually divided into four paragraphs: name(s), botany, herb nature and (contra)indications. In modern herbals the chapters are likewise divided but the paragraph on "herb nature" has been replaced by a paragraph on "chemical constituents". Therefore, we looked for a relationship between the "nature" of herbs in the past and the chemical compounds in the present.
To get a better view of this suggested relationship, several herbs allocated in the way most authors agree on, were combined with a simple therapeutic/chemical classification of herbs as given for example by Wagner (28).
Looking at the dominant compounds in these herbs in relation to their allocation to the four elements, the large digestibility reducing compounds (like tannins and large carbohydrates, the mucilages) are more often found in the "cold" region and the smaller toxic compounds (aromatic or iridoid) in the "warm" region. It seems consistent with the theory that 'cold' plants slow down and give rest to the human physiology, that we mostly find plants here that concentrate their defense on these compounds that stop diarrhea and ease the mucous membranes. Another thing that becomes clear is that the 'wet' effects of herbs can be attributed to smoothening compounds like water, mucilaginous compounds or fatty oils, and that herbs that are used because of their tannins will be considered "dry". The *Lamiaceae* family is well known for the combination of tannins and aromatic compounds, and many *Lamiaceae* plants are classified by all authors as warm and dry. Most *Rosaceae* members are allocated to cold and dry, in particular those with tannins that lack aromatic compounds.

Most medicinal plants have more than one important active compound, so different allocation of herbs can be a result of a different appreciation of their contradictory "natures". An example is *Plantago lanceolata*, known for both its astringent (tannins) and emollient properties. Probably Dodoens had observed both mucilages and tannins in *Plantago* leaves as he states: "It is of a mixed nature: cold/watery but also tart/earth-like: cool and dry."
The traditional way of preparation, bringing specific compounds into the foreground or background, also plays a role. The allocation of *Vitis* products mentioned before illustrates this. Another interesting example is the nettle (*Urtica spp.),* which has a lot of silicium and tannin in it, so that it could be cold (it is classified as such in China where preparations that have been boiled are sold). However, the presence of histamine in the fresh plant, and the burning sensation it gives when the living plant is touched by hand, is probably the reason why it is considered to be hot in Western herbals.

Discussion
This study was a pilot literature survey, it generated a few hypotheses that can be tested in follow up studies.
An interesting question that arises from the average values of hot, cold etc of all inventoried

herbs is whether the “temperature” of some plants is considered to be lower in herbals from the south of Europe (the warmer countries) and vice versa. It is striking that in the Italian work, hot and cold items are available in nearly equal amounts, whereas the German, Dutch and English herbals contain larger amounts of hot and dry plants. To make this observation conclusive, this theory should be tested with broader samples; now we have only one Italian sample.

Another question could maybe be answered by studying European Pharmacopoeia from renaissance tot the 20th century: Was the "temperature" of plants of influence on the development of chemical medicine? For example the discovery of the isolation of alkaloids like morphine and hyoscamin was hindered by the conviction of 19th century pharmacists that (these kind of) active principles were mainly acidic, like valerianic acid, not alcalic (as we saw before: they were of extreme cold and dry nature).

A very intriguing question is of course whether the allocations studied here currently still serve a purpose. Whilst choosing an herb for a specific patient, the herb allocation was related to the humeral constitution and condition of the patient. The elements were the vehicle of explanation for this correspondence. The “nature” of herbs was used as an explanation for their effects in an abstract level, in the same way that chemical compounds are used today. If we look at the way herbs were chosen, we do not find that it was general practice to “combat” the energy that is abundant by using an herb that has the opposite energy. More likely, some “missing” qualities were supplied. When one aspect was in excess, e.g., fire, herbalists would try to distract or dissolve this excess by using an herb low in fire and high in air quality. In addition, herbs were considered useful to help the body through the seasonal changes. For example, at the end of winter, there is much abundance of phlegm (giving rise to colds and influenza) so then a drying but moderately warm herb like *Lamium album* was prescribed. On occasions like this, one would not just grab the warmest and driest herbs at hand.

The allocation of herbs gave rise to contraindications for their use. For example, Culpeper and Dodoens warn readers that garlic, an extremely hot and dry herb, should not be used by persons with the same (i.e., choleric) temperament or constitution. In general, choleric persons can be helped with bitters to open and spread the energy, but they should not eat hot foods like garlic or pepper, as this will worsen their condition. Sanguine persons lose energy quickly, so they can benefit from tannins but should not use too much oil, fat, or bitters. Phlegmatic persons lack heat; they can benefit much from aromatic herbs but must not eat cold or slimy foods and herbs like cucumber or lettuce. Melancholic persons are very cold and inwardly centered so both warm and bitter herbs will serve them; for this condition, cold and dry herbs (oak) or food (vinegar, hordeum) are contraindicated.
These 'constitutional' treatments are still in use by Dutch naturopathic herbalists (probably also in other countries), but there has been no research into the effectiveness of this approach. As naturopathy is far from standardized and uses non-validated diagnostic techniques (such as iridology), only a black box approach is possible at the moment.

Ross (**6**) stressed the importance of taste for a medicinal classification of European herbals, but he analyzed the tastes according to Chinese traditional pharmacological principles. Our studies try to connect classic European herbalism to modern scientific findings. Even primates seem to prefer certain plant families above others (workshop 1A).
Recently in the Netherlands studies on TCM classification of patients into hot and cold patients appeared to have a clear relationship to their metabolic profile (29), so it could very well be that these indications and contra-indications looking old-fashioned may point us nevertheless a simple way to the so very much needed personalized medicine. Maybe also for animals, as I suggested in the workshop 1B.

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3. A. Homeopathic remedies and dosages in relation to the phytotherapy praxis

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Abstract

For some, even modern German and Dutch herbalists, the dosage seems to be of less importance than the herb choice. Here we see the influence of homeopathy, that values more the energetic/informative value of holistic herbal remedies as opposed to their material/chemical effects. In English speaking countries higher dosages are used; this tradition was influenced by the US eclectic physicians. Modern research on hormesis, adaptogens and carvacrol suggests that a small dosage may lead to an unexpected response.

Introduction

The first slide shows the front cover of a *hormesis* special we did with our Journal. It was not easy to visualize the concept of hormesis A book of Paracelsus, who is always quoted (dosage makes the difference between poison and medicine) we added to the picture. In the front it shows a test of some chemical reaction that is expressed as a red color, and so you see that a lower dose has a stronger effect then the dosage that is the beginning of a linear dose-response curve, whereas the highest dosage again gives no effect at all.
Before founding of the IEZ (in the beginning of the 90's) I was working as a post-doc for a foundation that wanted to stimulate the cultivation of garlic in the Netherlands and was based on Nijmegen University. There were a lot of fungal and bacterial problems in the garlic, and no pesticides or other methods of chemical protection were allowed. Therefore we researched the possibility to use homeopathic remedies on garlic plants, to grow them safe in the cold and wet Netherlands climate [1]. We had an extremely small budget and no results, so I did not make this to a topic of a workshop. But it made me wonder if it was possible to discuss peacefully some concepts of homeopathy with rational scientists from the modern world.

Hormesis: Paradoxal dose-response relations

A few colleagues of mine studied also in the 90's the phenomenon "Hormesis" on Utrecht University. Hormesis in biology is well known as the favorable biological responses to low exposures to toxins and other stressors. This phenomenon seems to be rather close to the "similimum" hypotheses in homeopathy. While trying to shed more light on this, my colleagues, although the research was sponsored by a homeopathy firm, had to avoid the H-word carefully as homeopathy is rather demonised by more powerful people in this university.

Recently the study of hormesis is again receiving attention. As the process of banning toxic substances from our food is becoming unprecedentedly severe by more and more EU safety rules, professor Aalt Bast from Maastricht University was cited in several Dutch media, when he referred to this phenomenon with the claim: Poison (in a small amount) is necessary for our health. Indeed this seems to be the case.
In 2012, researchers at UCLA found that tiny amounts (1 mM, or 0.005%) of ethanol doubled the lifespan of *Caenorhabditis elegans*, a round worm frequently used in biological studies. Higher doses of 0.4% provided no longevity benefits. At the same time mild stress exposure appears to have anti-aging effects. This is used to explain the beneficial effects of moderate exercise, but also the beneficial effects of (certain toxic compounds in) herbs.
Other examples of the hormesis principle would be the life extending effect of calorie restriction (fasting); hypoxia, (small doses) cytostatics, mild oxidative stress, heat shock.

When I studied naturopathy (1980-85) I did both courses, on homeopathy and on herbalism, and I was fascinated by the herbs that appeared in both therapies. It is clear that coffee wakes you up whereas homeopathic coffee preparation is supposed to make you sleepy.

But in phytotherapy *Valeriana* root is used for sleeplessness, and in homeopathy it is the same. How was this possible? And I discovered more and more herbs with the same indications in phytotherapy as in homeopathy (*Cimicifuga, Chamomilla, Echinacea*). Another thing I found fascinating was that these herbs, taken in overdose, reproduced the ailment that they should dissolve. Overdose of *Valeriana* gives valeriomania, whose symptoms are much like the homeopathic indication. I had an interesting experience with *Chamomilla* when a house mate overused the tea of this healthy plant. He developed jaundice symptoms. So I wondered: are we taking these herbs actually in a dosage that belongs to the hormesis-range?

Adaptogens

Nowadays some herbs are called adaptogens. An adaptogen is a herb that longens the lifespan, probably by adding a bit of stress, just like a tiny bit of alcohol. It seems logical to study them also in the *C. elegans* model, as my friend of Utrecht University did (2). Wiegant wrote in a paper about plant adaptogens (*Eleutherococcus senticosus* (SHE-3) and *Rhodiola rosea* (SHR-5)) that they are able to modulate the normal lifespan of *C. elegans* in a dose-dependent way. The most efficient concentrations were able to increase the mean lifespan with about 15%, whereas higher concentrations had either no effect or even shortened the mean lifespan. Interestingly, the mean lifespan could also be increased when these adaptogens where added later in life. Apparently, it is 'never too late to start' exposing worms to adaptogens in order to increase their lifespan. In addition, an increase in stress resistance was observed when worms were incubated in the presence of adaptogens.
Now these observations raise a number of questions, as Wiegant and his co-authors point out.
- Are adaptogens unique as plant products that increase the mean lifespan of *C. elegans* ? No. It was recently showed that *Rhodiola rosea* was able to increase the mean lifespan of *Drosophila melanogaster*. In recent studies it has been demonstrated that also other extracts or isolated compounds from plants like *Ginkgo biloba,* blueberry extracts and its polyphenol fraction as well as resveratrol from the *Rhodiola rosea* (SHR-5; 25–100g/ml) induce the specific molecular (gene) responses that Wiegant found in his research. Some adaptogens and heat shock induce the same kind of gene expression. Responding to a heat shock the cells synthesize HSP (heat shock proteins) for cell repair; this response was also seen when immune cells were treated with carvacrol (3). Carvacrol, an important compound of oregano- and thyme-oil, has strong antibiotic properties and it is used abundantly in feed for farm animals in Europe.
- Maybe adaptogens may cause DAF-16 localization in an indirect way due to caloric restriction (that is known to affect DAF-16 localization and to induce lifespan prolongation)? Maybe adaptogens kill or affect the growth of bacteria that serve as food source of the worms throughout the experiment? No, bacterial growth was not affected by adaptogens.
- How do plant adaptogens prolong lifespan? Plant adaptogens were able to interfere with the localization of the DAF-16 transcription factor. DAF-16 is considered to be a crucial transcription factor in stress resistance and lifespan determination. It was shown that adaptogens induce a nuclear localization of DAF-16. Once in the nucleus DAF-16 initiates the transcription of a large number of genes involved in metabolism and oxidative stress resistance, including chaperone's and detoxifying proteins, which may explain a change in the rate of aging and longevity. It has been shown that mild stress (including heat stress, oxidative stress and caloric restriction) induce a nuclear localization of DAF-16.This raises the intriguing question whether adaptogens exert their beneficial effect by inducing some mild stress first. In this respect it is of interest that recently a pro-oxidative action of the adaptogens in cells in culture was demonstrated. These results obtained in cell cultures were concentration dependent. Low doses enhanced the antioxidative defense, whereas higher doses of adaptogens were shown to cause oxidative damage leading to cell death. An anti-oxidant can (when saturated) also respond as a pro-oxidant and then become dose-dependent beneficial or damaging for the health, this is a great problem when researchers want to assess health benefits of vitamins and other supplements. The phenolic components

present in plant adaptogen extracts may also exert an anti-oxidative action that could explain the observed life-span prolongation. Both the anti-oxidative and the pro-oxidative potential of a variety of beneficial dietary compounds (including phytochemicals such as resveratrol and curcumin) have been discussed in which a beneficial effect of the pro-oxidative action of these nutritional components is usually explained in terms of an induction of anti-oxidative endogenous defense mechanisms.
- Do adaptogens resemble hormetic components in their mild stress action? The initial beneficial effect and subsequent adverse effect of both adaptogens suggests and resembles a hormetic action. More detailed comparison of effects at the cellular and organism level are required before adaptogens can considered to be hormetins, concludes Wiegant, but I think this hypotheses deserves further consideration; it seems likely we are looking at the same stimulus-response mechanism here. And this may also be the case with homeopathic remedies in their mode of action.

From material to informative dosages
The *hormesis* principle is quite similar to the *similimum* principle of the homeopathy. Dose-response is averse; a lower dosage will give (at some occasions) better results than a higher dosage. Of course the question remains how low the dose can be, before the effect of a dilution will be gone. In this light it may be of interest to read some parts of an article I wrote in the 90's, whilst engaged in researching homeopathic remedies in plants (1), addressing these questions:
How can high potencies have any effect if all the original chemicals are diluted out during the preparation? What is the difference between water and for example the homeopathical substance Phosphorus C1000, a preparation in which the original substance is diluted to 10^{-2000}, a standard preparation for a classical homeopath? Apparently it isn't a chemical or the temperature. Hahnemann, the founder of homeopathic medicine, called his preparations "dynamisations", and their point of impact would be the "dynamus", otherwise known as life force or vital force. Nowadays we speak of the self-healing ability that can be specifically stimulated by a certain homeopathic preparation. The homeopathic remedy is viewed as an information transmitter, a "message in a bottle". By providing the organism with information concerning a specific poison (while the toxin itself is barely or not at all present) it corrects itself in order to deal with it, and takes on certain adaptations to cure itself of a different disease (of which the symptoms are comparable to the symptoms caused by the toxin in the remedy in high doses). But how can specific information on a poisonous compound remain in, or with the "carrier" (the homeopathical preparation), after many dilutions?
First we will have to realise that *information* is a totally different life force than chemicals or energy. For example it is non-quantititve. Energy-units can be added-up to their sum, or dividable to for example half of their quantity. This "law of conservation" doesn't go for information: two maps of the same town do not give more information than one. Information has a redundancy aspect and when divided by two the quantity doesn't decrease, but stays the same. Some have remarked that catalists (enzymes in living organisms) could serve as a model here. They are necessary but not used up for certain processes. Information is a part (an extra dimension?) of every object in this world, and is not absent when there is no material (left) but the transport of information between sender and receiver, and the coding involved in this transport, is the real study object here. Think of the very illustrative example Gregory Bateson gave: The letter you DIDNOT send, that made your mother angry!

Homeopathic and phytotherapeutic preparations as "information carriers"
When we try to keep an open mind for "informative" aspects of matter the debate on low or high potencies and simplex or complex-remedies will be less heated. The preparation of a homeopathic remedy consists of step by step diluting and shaking. With this people assume that after the D24 or C12 no molecules of the primary substance are left. This however has never been proved; there is simply no measuring equipment in physics that could determine that. A physics professor once pointed out the possibility to me that this specific way of preparation might prevent the last molecules of the primary substance to disappear. That

organisms can be extremely sensitive to a single molecule with a strong informative value is no news. And the dispute about “remedies that contain nothing” is ludicrous. Water that “contains nothing” hardly exists. If you stir or shake milli Q water whilst measuring the pH value and you sigh you will see the pH value shoot up. And all kinds of metals let go of the glass sides of the bottles. Despite classical homeopaths preference for “simplex” remedies it is hard to imagine how these “simplex” start and stay "simplex". Just look at the ingredients indication on a lab-"pure" jar of Natrium Chloride (Nat mur for the homeopaths). The available “pure” primary start substance is are always slightly contaminated.

On the other hand, if herbal medicines (adaptogens) are used as hormetics, there is a common ground where herbs meet homeopathy. Can a small amount of a substance (homeopathic low potency) still be of influence when at the same time the substance is present in a more normal dose? I met a scientist in Italy (Speciani) whose research (4) has shown that this is sometimes possible. He experimented with been-sprouts that were infected with a fungus. Administering 2,4 D (1/10000 M) slowed down the infection, but the infection slowed down a lot more when administering a C5, C6, C7 or C8 potency of 2,4 D at the same time. This remarkable result suggests that the preparation does make a difference. It would be interesting to repeat this research and, if it works, expand it to higher potencies.

The way an organism reacts to a poisonous substance does of course depend on the dosage. But not necessarily a low dosage means a low response, as we saw in the adaptogen example. That a small dose of a damaging agent can offer protection from a larger dose later on, is a well known occurrence (vaccination, immunisation). Less well known is that a small dose, administered during the recuperation process of a large (but not lethal) dose, can benefit recuperation. This has been demonstrated on cellular/molecular level at Utrecht University by van Wijk and Wiegant in1994.

There are in Europe (in particular in the Netherlands and Germany) a lot of phytotherapists that work with extreme low dosage phytotherapy; they are probably strongly influenced by homeopathy. Unfortunately there is little scientific interest in these practices. The only research publication in this realm that I know of is of Kalbermatten (Germany) who has a rather anthroposofic view on plants (5,6). This study, with *Solidago,* where the more diluted homeopathic tincture had a two times stronger diuretic effect as a 10fold concentrated phytotherapeutic tincture. The study was interesting but old, methodologically weak and never repeated.

Another aspect of phytotherapy research might be of interest in the light of the homeopathic tradition. Homeopathy uses mainly tinctures of the whole plant as a starting point of the preparation of remedies. Phytotherapy research often shows that a lot of isolated compounds alone or in combination do not provide the same effect as a complete extract (7). If this is the case, this might point to a remedy that has a high informative value and can be used in an extreme low dosage (i.e. in homeopathy). We could argue that the phytotherapeutic use is in the hormesis range; and so indications are more or less the same for homeopathic and phytotherapeutic use of this plant.

The hormesis concept has had many difficulties to gain acceptance in the scientific community, due to the connection Hugo Schulz made to homeopathy (8). Calabrese was very unhappy with this.

Discussion

It may take many years before science gets a grip on homeopathy and may give it confirmation equal to the way science has supported phytotherapy. If so it might be necessary to change also some traditional homeopathic views about for example the simplex

mineral remedies. It may also be that homeopathy splits into two practices, one being low dose (*hormetic)* phytotherapy; the other being purely informative, using maybe some kind of bioresonance equipment. Maybe it will be a discipline within psychology, intentional healing, who knows.

In this workshop additional and conflicting views of the participants regarding the hypotheses described above are welcomed.

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3. B. Ethnoveterinary research: old remedies and their validation
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Abstract
Traditional use of herbs for animals can be found in farm handbooks from circa 1500-1900; afterwards chemical synthetic medicine gained popularity. Herb use in the Netherlands, Germany, Austria and Switzerland was very much influenced by the Mediterranean tradition. A lot of herbs were (and are) given to animals for similar conditions as in humans. Specific aspects of animal application are amongst others the influence of herbs on the rumen flora. Ethnoveterinary research demands (like ethnobotany) a respectful attitude towards the informer, interest in the traditional philosophy behind it and specific methodology. Validation steps for traditional remedies include documenting international use, pharmacological research, clinical experience, Randomised Controlled Trials..

Introduction
Veterinary schools were founded in Western Europe between 1762 and 1821, concentrated on horses and owed much to farriery. Until that time sick animals were treated (if at all) by their owners. For expensive horses the family physician was called.
Human phytotherapy can refer to published knowledge and experiences over a range of thousands of years. In old herbals sometimes we find reference to the treating of animals. In 1873 Gillet-Damitte, in a communication to the French Academy, stated that *Galega officinalis* (goat's rue) when given to cows would increase the secretion of milk from 35 to 50 per cent (according to Grieve). About *Rauwolfia serpentina* in old Indian legends it was said that mongooses eat the Indian snakeroot as a protection from venom before they battle cobras in the jungle (actually a zoopharmacognostic observation), therefore it was used against bites of insects and snakes. Specialised animal herbals we find in Europe from 1850 onwards. One of the most famous might be the 1952 *Complete Herbal Handbook For Farm And Stable* by Juliëtte de Baïracli-Levy. She observed the use of herbs by South European farmers and gypsies, this may be one of the first ethnoveterinary studies. Even nowadays these regions offer interesting data on herb uses for animals (1).
Ethnoveterinary research was defined in the 1990's by Mathias and McCorkle, who edited several text books about this interdisciplinary science. They named it: the holistic, interdisciplinary study of local knowledge and its associated skills, practices, beliefs, practitioners, and social structures pertaining to the health care and healthful husbandry of food-,work- and other income-producing animals. Evelyn Mathias, a German vet, always emphasized that this is not just about herbs.

Where to find ethnoveterinary remedies?
Two obvious roads are possible: older agricultural (cattle) handbooks or field work in (several) contemporary cultures. Sometimes they overlap.

1. Reviewing traditional literature.
* In agricultural handbooks of the 18th and 19th century there are several herbal recipes given. Several of them (in German language) were analyzed considering the modern knowledge of medicinal active plant compounds by students of the Veterinary University in Vienna (2,3).
* Hubert Karreman, experienced organic cow vet, mentions remedies with indication and doses citing a table made in 1930 by Dr. Fish, Cornell university (4).
* In the East of Europe for a long time private pharmaceutical industry was not welcomed by the communist government and therefore herbs remained important as animal medicine for a long period. For example the pharmacology study book of the veterinary university of Leipzig (Eastern Germany) in 1989 included many herbs and less synthetic drugs than the West European books. The practical dosage information from a small booklet of the Russian professor Rabinovich (5) was important for German scientists that aimed at re-introducing herbal medicine in the veterinary practice at the start of the 21st century.

2. Field work (applied anthropology).
* Many consider Juliëtte de Baïracli-Levy (1912-2009) to be the mother of all ethnoveterinary research. Every year I show to new students a beautiful documentary of her life and work that was made in 1999 by Tish Streeten. As much as I respect her work I consider it a pity that she did not refer more detailed to her sources, only in general terms (mainly for example: the gypsies use this). Nowadays it is good practice, for example in India where much etvet work is done, to name with each remedy the person that helped to include it in the study (often a traditional healer). Organizations like ETC/Kompass do this to prevent biopiracy.
Use ethnobotany methods: free listing, calculating (cognitive) salience index: S = F/N.mP where F = frequency = number of lists in which item is mentioned; N = the number of lists you have collected; mP is the mean position of the item on the lists (rank; for example if it is mentioned by one as first, by another as 7th, by another as 3th, it would be 11/3=3,7).

* An interesting fact is that problems in the 3rd world relate to farmers problems in the richer part of the world: in the latter the farms are bigger, but farmers often nearly as poor! For example the average farm income in the Netherlands in 2009 decreased to 15,100 euros per farm, this is nearly the lowest acceptable income for Dutch citizens (€ 1284,-/month in 2009). A summary of the Dutch history of enlargement and enpoverment of farms can be found on www.dutchfarmexperience.com, the website of Katrien 't Hooft, a Dutch (ex-ETC) vet. Anthropologist Cheryl Lans is building bridges between ethnovet practices in different countries. She has done participant observational work, both in Trinidad & Tobago and in British Columbia. Ethnoveterinary medicines used in Canada are mainly derived from Europe, the First Nations and American Indian traditions and from Asia [6,7,8]. This was also concluded in the survey IEZ made in the Netherlands [9].

* In the Netherlands Wageningen University (WUR) is the only research institute that gets funded by the Dutch government to address agricultural questions, also regarding organic farming. Most WUR researchers are unwilling to share this money with more specialized private research organizations like IEZ, the Louis Bolk Institute (LBI) or others. WUR has made inventories of the herbal and other natural products that organic farmers use for their cattle and also made literature-based advices on herb use. Further in the text a few examples will be given of some problems that arose from the WUR-approach.

How to validate the remedies?
Again two ways are possible: experimental or non-experimental validation.

1. Experimental validation
* It will come as no surprise that experimental validation that not involves experts on traditional herbs, as in many cases in Wageningen University (WUR), results negative. A striking example was a study that van Krimpen et all performed [10,11]; it was commented on by Lans [12]. Before the trial pharmacognost advice was sought on what herbal remedies to test to combat *Ascaris suum* (roundworms) in pigs. After a literature search the advice given was (amongst others) papaya latex, this is a specific product that can be made from unripe fruit or leaves of papaya tree. For economical reasons Van Krimpen used the papaya ripe fruit juice (a cheaper product, but without anthelminthic activity) to perform the experiment. The original pharmacognost advice was neglected, and he was not asked to contribute to the publication in the Veterinary Parasitology Journal, that was criticized by Lans [11,12].
Van Krimpen et all wrote that they also tested the herb *Artemisia vulgaris* [11]. However, they referred to literature on *A. brevifolia*. During a presentation on this research in a meeting of the Netherlands Association of Phytotherapy (NVF) it became clear that the lead author Van Krimpen could not tell what *Artemisia* species he had used for the experiment (he had ordered *Artemisia*, not specified, from a supplier). As there are many *Artemisia* species in the market, with big differences in application (from kitchen herbs to the effective anti-malaria remedy *A. annua*), the exact species used is an important factor in the study. Although in the

Van Krimpen study a beneficial influence of certain herbal products on liver spots was clearly visible, being non-significant different both from negative as from positive control, this general conclusion was written as if his results were very negative for the use of herbal products [11].

* Some interesting examples of experimental validation of ethnoveterinary remedies were published by WUR, always by MSc or PhD students from outside of Europe that spent a few years in the Netherlands to complete their academic study. This concerns for example a proven beneficial influence on growth performance and on the immune system of broiler chickens in an *Eimeria* challenge by the mushrooms *Lentinus edodes, Tremella fuciformis* and the herb *Astragalus membranaceus* (Fucun Guo, China, 2005) or the combat of brown ear thicks in cattle by aromatic plants from Africa such as *Tagetis minuta* and *Tithonia diversifolia* (Wycliffe Wanzala, Kenya, 2009).

* A textbook on ethnoveterinary botanical remedies was edited in 2010 by the South Africans Katerere and Luseba (13). It focuses strongly on experimental validation, non-experimental validation as a method is not mentioned, nor are the previous activities of Mathias and McCorkle (or Lans).
In South-Africa the work of Kobus Eloff is interesting. In 2012 he wan a Billiton award and since then you can find several international lectures of him on YouTube. He has a big phytomedicine (ethnoveterinary) program running on the Veterinary Faculty of Pretoria, aiming to enable the use of medicinal plants growing in South Africa, particularly from Combretaceae family, for the benefit of its people and animals. The program investigates problems in the wide area of infections, especially microbial and parasitic infections in the process of training postgraduate students and uses mainly bioassay-guided fractioning methods.

2*. Non-experimental validation*
* Non-experimental validation is an aspect of applied anthropology, says Lans [6,7,8,10]. It is much cheaper (and so more cost effective) than experimental validation as the latter benefits more the scientists and their institutions, whereas the former with the right methodology (participating research) benefits the farmers most.

Ethnoveterinary related activities take place in every society, but in the Netherlands they are undertaken by universities that didn't build up or hire expertise on ethnoveterinary ethics and methodology. There are some disadvantages connected to this situation, as the following examples show.

The agricultural University of the Netherlands in Wageningen (WUR) was asked several times to make inventories of ethnoveterinary ('alternative') remedies used by (mainly organic) farmers. They did this without involving proper ethnoveterinary or related herbal medicine expertise. Three examples, taken out of the resulting reports, are given here:

1.One WUR study [14] mentions the use of "alternative medicine" on 27 out of 30 farms, of which only 1% is phytotherapy. The report lists phytotherapy use without giving a proper definition of phytotherapy. The small amount of herbal remedies (on page 27) is mainly due to a lack of knowledge, as many herbal remedies are listed under the "general" category (phytotherapeutic registered remedies like Uterale/Sabine herb and all volatile oil based products of *Mentha, Eucalyptus, Thymus, Melissa* and other species) or as a homeopathic remedy (*Echinacea*).

2. Kijlstra [15] in another WUR study on page 39, mentions a remedy used by goat farmers for wounds "Titrie", without further specification. Any herb expert would have understood that it should be Tea tree (*Melaleuca* spp.) The inclusion of this important, well documented remedy in this way is useless in Kijlstra's report.

3. Mul and Reuvekamp [16] published an overview of herbal remedies for poultry worms. With this aim they made an inventory of relevant literature, both ethnoveterinary field work and experimental lab work. The report shows many methodological and linguistic shortcomings. The authors give only 4 literature references in a report mentioning ca 200 plants. Some of the plant names are given with the author who mentions them and the year of publication, but without the actual references. Other plants are mentioned with no indication for a reason. The decision on what to advise their target group (organic farmers) to do regarding future research is based on a kind of non-experimental validation i.e. a judgment (no criteria mentioned) by the two authors with no other experts involved of the (not given) reference publications. Criteria such as 'locally and cheap available and non-toxic' and 'both *in vitro* and *in vivo* data should be available' were used to select a number of plants that should be further examined. Of these 5 plants St John's wort (*Hypericum perforatum*) was excluded because of reported side effects (no references given).
A small part (randomly taken) of the long plant list that forms the body of the publication is copied here:
Echinacae …. Zonnehoed
Embelia schimperi
Emblic myrobalans Ambla
Eucalyptus Gomboom, Gums onbekend nee VIVO olie (waarvan?) Mocsy 1931 AB
Euonymus europaeus Wilde kardinaalsmuts, Spindle
Euonymus verrucosus
The first, third and fourth plant names in this list of six are wrongly spelled and/or not identifiable on a species level. As no references are given by all but one (and this is a very incomplete reference) it remains unclear what the source is of these mistakes.

The fact that nearly all government funded research regarding (both organic and regular) livestock in the Netherlands is performed by WUR-LR (in general, no open competition between research institutes is organized) makes it clear that methodological failures as mentioned above cannot easily be improved.

Methodology for ethnoveterinary participating research
The research process as described here short and stepwise, was used by Lans (7,8,10) and is here cited from (10).

Identification of practices
Compile a list of livestock farmers and other informants.

1. The sample size should be appropriate.
2. All participants should be given consent forms prior to participation in the research.
3. A draft outline of the participant's ethnoveterinary remedies is discussed during a participatory workshop in order to establish that dosages were accurately noted, for input on content, and to clarify any points.
4. The participant-approved drafts are compiled into the draft manual to be discussed on the last few days of the workshop.
5. Medicinal plant specimens are collected where possible and these are identified and deposited as vouchers at the closest herbarium. A voucher herbarium specimen is a pressed plant fully annotated and placed in a Herbarium for future reference.
6. Interview schedules are filled in accordance with published guidelines (see 10).

Validation of practices
The research team completes the non-experimental validation of the remedies in advance of the workshop. Traditional validation and drug discovery is extremely expensive so a non-experimental method is used. This method consists of:
1. obtaining an accurate botanical identification

2. determining whether the folk data can be understood in terms of bioscientific concepts and methods
3. searching the chemical/pharmaceutical/pharmacological literature for the plant's known chemical constituents and to determine the known physiological effects of either the crude plant, related species, or isolated chemical compounds that the plant is known to contain. This information is used to assess whether the plant use is based on empirically verifiable principles or whether symbolic aspects of healing are of greater relevance. For example if the plant is reputed to cause itching or bleeding, the assessment determines if it contains chemicals that can cause itching and bleeding.

If ethnobotanical data, phytochemical and pharmacological information supports the folk use of a plant species, it can be grouped into the validation level with the highest degree of confidence. There are four levels of validity (17):

1. If no information supports the use it indicates that the plant may be inactive.
2. A plant (or closely related species of the same genus), which is used in geographically or temporally distinct areas in the treatment of similar illnesses, attains the lowest level of validity, if no further phytochemical or pharmacological information validates the popular use. Use in other areas increases the likelihood that the plant is active against the illness.
3. If in addition to the ethnobotanical data, phytochemical or pharmacological information also validates the use in European or North American tradition, the plant may exert a physiological action on the patient and is likely to be effective.
4. If ethnobotanical, phytochemical and pharmacological data supports the folk use of the plant, it is grouped in the highest level of validity and is most likely an effective remedy.

Validation workshop

The workshop that is an essential part of this method (18) involves participatory documentation and validation of the previously recorded ethnoveterinary remedies together with research participants comfortable in talking about their practices. Information on pre-selected ethnoveterinary practices will be prepared in advance for the workshop and working drafts of topics based on each farmer interviews will be given in advance to farmer participants for critical review. This will avoid unnecessary overlap in the participatory workshop. In the workshop the facilitator asks participants very specific questions in a supportive environment about the medicinal plants used. The group interaction is said to produce data and insights that would be less accessible without the interaction, it can refresh memories and encourage sharing. After the first presentations and discussions, the materials are edited, and the first draft published by the workshop staff. This draft is then critiqued and modified by the group. This process can be repeated on each of workshop days. During the last day, the research team discusses the final draft.

At the end of each description there is a number in parentheses with these meanings:

1. Standard veterinary practice or equivalent
2. Traditional practice supported by scientific knowledge
3. Traditional practice that animal healers acknowledge and agree works.

Practices not rated according to 1, 2 or 3, will be rejected.

The final draft of the manual should be ready shortly after the end of the workshop and then published. The manual should consist of easy-to-read, simple information on low-cost, locally available ethnoveterinary practices that can be applied in the developed world. To prevent biopiracy the input is documented together with the source of the remedies (informant, mostly farmer or healer)

Discussion

Many so called innovations in science have been farmer's wisdom for ages. Unethical and unmethodical ethnoveterinary studies can lead to failure and also to biopiracy.

I hope to demonstrate some ethical and practical aspects of ethnoveterinary research in the workshop and discuss the various methodologies with participants.

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4. A. Registration and marketing (perspectives) of herbal medicinal products in Europe
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Abstract
Very few farmers in Europe grow herbs to treat their animals the way farmers used to do traditionally. Specific products have been developed, some by farmers, some industrial. Examples will be given of
- herbal medicinal products for animals (they have become rare in Europe as the registration is too expensive)
- herbal feed additives (mainly registered for taste improvement but range of action is larger; e.g. Indian herbs)
- herbs as feed ingredients or supplemental feed (a booming market, both in pet food and in agriculture)

Introduction
The market for herbal (medicine/feed) animal products in Europe has had a boost by the 2006 ban of antibiotics in feed in the EU [1]. Still it may be complicated for a non-European company to enter this market as there are three very different channels .
Paradoxically there are next-to-none new (21st century) registrations for herbal medicines, or for that matter, for natural product-medicines in general [2].
On the other hand, the inclusion of herbal products and other natural products such as inulin, diatoms earth, enzymes, organic acids in feed additives is really booming.
The third possibility, the inclusion of herbs as a feed material is hardly regulated, and all medical claims must be left out. It is used a lot, but it is rather invisible.
We will discuss all three routes in relation to animal herbal medicines and health products.

Registered herbal animal medicines
The office that provides a license for the distribution (=registration) of an animal medicine is the same office (yet another department) that gives these licenses for human medicine. In Europe it is called EMA (European Medicines Agency) and in the Netherlands CBG-MEB (Medicine Evaluation Board). Each country has its own office, Germany for example has the BfArM. Registration of a new animal medicine is an expensive process. New EU regulations have made this harder rather than easier. Therefore registered herbal medicines in Europe at this moment are mainly old registrations. In the Netherlands they can still be renewed, as long as no problems appear in veterinary practice or in the food chain.

In Germany however, a country with a rich history of animal herbal medicine, the German BfArM has forced all suppliers of animal medicine to meet all modern EU legislative demands; as a result they had to do new research with their old medicines. In most cases this was not financially viable and many of these products are now sold as supplementary feed or care products for animals. The basis for the use of functional plant extracts in feed is their registration as feed additive under EU Reg 1831/2003 where a lot of these extracts had a preliminary legal status as feed flavoring substances. With the thorough evaluation of the dossiers most of them will not be able to meet the requirements for documentation and will not be available any more. Hardly any firm will register a new herbal medicine for animals at this moment, high costs making it unattractive. Only a few exceptions exist in Germany: a Neem extract against sheep fleas was registered in 2013 but the respective tests were done many years before. And to my knowledge one firm in Kempten (Bayern) is still intending to acquire a new registration for a veterinary medicine based on a plant extract but failed so far.

Registration demands for small pets are not as strict as they are for consumption animals, as there is always the issue of safety for the human consumer in the latter case. Foodstuffs obtained from food producing animals treated with veterinary medicines must not contain any residue that might form a hazard to the health of the consumer. Before a veterinary medicine intended for food-producing animals can be authorized in the EU, the safety of its substances

and their residues must first be evaluated. Therefore the maximum concentration of residue (MRL) and eventual withdrawal times for slaughter have to be evaluated.
When it comes to herbs and other natural products, the problem is often that (nearly) the same products are sold as feed ingredient or feed additive; without the high costs for registration, but still effective. That is the reason the EU created an easier registration of herbal products for human use through the THMPD (Traditional Herbal Medicinal Products Directive). EMA makes herb monographs that summarizes (nearly) all knowledge on effectiveness of the herb and also specifies the technical requirements that must be met, related to the claims that are expected. This is a step forward in the emancipation of herbal medicine, but - unlike the situation for synthesized medicines - registration is not central for Europe but has to be done in the separate countries. Alas, for animal medicine this way of registration is not open (yet?).

Feed additives
Animal feed additives are regulated by Regulation EC/1831/2003. Feed additives are products used in animal nutrition to improve the quality of feed and the quality of food from animal origin, or to improve the animal's performance and health. In the past antibiotics were a common feed additive. Feed additives can only be put on the market if authorization has been given following a scientific evaluation demonstrating that the additive has no harmful effects, on human and animal health and on the environment. So the feed additives have to be registered before they come to the market and the legislative association is not the EMA but the EFSA (European Food Safety Authority) [3]. The long list of plant extracts added to the Community Register of feed additive in 2005 consisted of a list of notified plant extracts listed under the functional group: “aromatic substances”. Hundreds of plants were listed, but in 2013 many have been removed [4]. As soon as a curative of preventive action is claimed, a product falls under the legislation on veterinary medicines. A EU country can only permit a veterinary medicine onto her market when the active substance(s)/product(s) in the product is placed in Appendix I, II or III of Regulation EEC/2377/90. Most herbs and from herbs derived products are placed on Appendix II and for none of these herbs MRL’s (maximum residue limits) have been set. The criteria used to place these herbs in Appendix II are very unspecific and variable.

Allthough it is obligatory for organic farmers to apply homeopathic and herbal medicines whenever possible, their use of (and innovation in the domain of) medicinal herbs is not very frequent. On the other side many regular farmers have started using products with herbs, probiotics etc. Some had experienced their children being refused in hospital as they carried multi-resistant bacteria. Others were convinced by their feed suppliers, that in their turn were convinced by feed additive producers that are working since long for replacing alternatives. Several EU projects were started where feed additive companies with scientific institutions explored the possibilities [5]. A current problem is that feed additives (even if they are 100% natural such as herbs or aromatic herb compounds) are not allowed in the growing market of organic agriculture.

Herbs as a (non labeled) feed compound
The feed industry in the Netherlands is comprehensive and it is relatively free in composing the feed. Producers have to declare no ingredients but just the general data such as carbohydrate %, protein content, fat % etc. Dried (milled) herbs do not have to be labeled specifically, just as "herbs & spices”. Any herb may be added. Without medical claims herbs can be used in animal fodder (feed), provided they are safe and not mentioned on the list of undesirable substances of the European Directive 2002/32/EC, and provided they do not contain toxic substances above permitted levels.
Currently new laws are being proposed in the EU which will give more restrictions, as they are holding a positive list (with allowed substances) [6].
Their are some farmers and other professionals with an agricultural background who sell specific herb mixtures (local home receipts) to farmers, sometimes through their feed

suppliers. Sometimes they are provided as an alcoholic tincture, which makes it illegal if sold to farmers directly (no extraction methods allowed) but it may be added by the feed supplier. Another problem is that the producer may not communicate the target health effects of the herbal mixture because officially it is 'just feed'. Not even a reference to a scientific investigation into the same product is allowed.

Examples
- Registered animal medicines: Uterale (with Sabina), Colosan (with fennel, cinnamon, aniseed, and carvi-oil); Cai Pan udderbalm (with Japanese mint)
- Feed additives: Digestarom (10 herbs), De-odorase (yucca) , Ropadiar (oregano oil, diatomeous earth), Enteroguard (garlic/cinnamon), Calsporin (Bacillus subtilis, probiotic)
- Feed ingredients: Bio-MOS (yeast cellwand; prebiotics), Cichoria-roots (inuline, pectine); Biomuehle Herb mix, Duo-elixer.

Bottlenecks
This paragraph cites the Fyto-V report [2].
Bottlenecks for the use of herbs in animals have not so much to do with the substances themselves, but more with the claimed efficacy. As soon as a curative or health promoting action is claimed, herbs are no longer regarded as feed products. All herb extracts notified as feed additives are categorized as aromatic substances and the only claims that can be made are taste and appetite improvement.
With other claims, the use of herbs would fall under the zootechnical additives together with other substances that improve functioning of the gastrointestinal tract. But under this category nothing is placed in the Community Register of feed additive yet.
The requirements for registration of veterinary medicinal products are aimed at single synthetic substances. Complex herb extracts cannot comply to the quality demands for composition, and the fact that all components of a herb need to be declared quantitatively. Not all components of herbal plant extracts are however known (and neither are those of feed products). Also, combinations of herbs are seen as complex veterinary medicinal products. In that case, the efficacy of the combination must be proven to be better than that of each of the individual composing elements. Other bottlenecks are the high financial costs and the ever stricter criteria that are used in the registration procedure over the years. The herbal substances that are registered now concern old veterinary medicinal products with registration dossiers that probably would not be accepted today.
For farmers who want to use herbs for their animals in a rational way it is necessary that herbal preparations with a reliable efficacy are available, which are safe for both humans and animals. It must be prevented that (farmers)deception occurs due to herbal preparations in which low or non-active doses are present and that are being praised with claims that are not substantiated.

Discussion: increasing awareness and commercial activities
We hope the Fyto-V project (discussed in workshop 4B) has contributed to the increase of activities and innovations that we see in the production and use of herbal products for farm animals. Of course, the ban on antibiotics in feed was a trigger, as is nowadays the concern about (multi)resistant bacteria.
Organic farmers are starting to grow more herbs in their field, and (phytotherapeutic) trees in the animal enclosures (as we discussed in workshop 2B). As IEZ we are now (at last!) asked to give advice on subjects such as herbs for aggressive male animals; herbs for transport stress, etc.
Globally, the Netherlands are an important player in the feed industry, and currently oregano oil is part of the feed nearly everywhere. In pet food the inclusion of herbs is becoming more and more fashionable. The inclusion of some NIS states in the EU has also triggered the awareness of the power of herbal products for animals. (NIS=New Independant States as they are called in their own edition of the WHO-monographs on medicinal plants).

For the NVF, Netherlands Association of Phytotherapy, one of our vets and myself are coordinating a project of 13 SMC's (small or medium sized companies) that concerns innovations in regular pig and cattle farms aiming at banning the use of antibiotics. Herbal products are involved, but also bacteria (*Bacillus subtilis* mainly) that are being used for the stables and for the farmers and coworkers. This situation is urgent as more and more farmers experience their children being denied access to the hospital.

It is my impression that natural products are gaining more and more influence as a part of the solution of the many problems we face nowadays in our society [7]. After many years of being considered a problem by regular scientists and vets this surely is a relief.

Depending upon the professional interest of the visitors of the workshop we can get into more details concerning specific cases or examples.

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http://ec.europa.eu/food/food/animalnutrition/feedadditives/comm_register_feed_additives_1831-03.pdf
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Rumen up and REPLACE (dairy cows; herbs replacing AB)
http://www.rowett.ac.uk/rumen_up/ http://www.replace-eu.com
Safewastes (medicinal re-use of plant waste) http://ec.europa.eu/research/health/infectious-diseases/antimicrobial-drug-resistance/projects/069_en.html
Planty http://www.planty-project.net/1.html and see also (about food/health)
http://www.ifr.ac.uk/sfc/research/default.html and Feed for Pig Health:
http://ec.europa.eu/research/biosociety/food_quality/projects/031_en.html
Feedseg http://cordis.europa.eu/projects/rcn/83985_en.html
BIOBIO http://www.biobio-indicator.org (biodiversity project)
FLAVO (about flavonoids in food)
http://ec.europa.eu/research/biosociety/food_quality/projects/073_en.html
FIBEBIOTICS http://www.fibebiotics.eu (fibers and the immune system)
NAMASTE http://www.namaste-eu-india.org (EU /India cooperation)
AGROCOS (www.agrocos.eu): Discovery/inventory of plant derived small molecules with potential as cosmetic/agrochemical agent.
NATPROTEC (www.natprotec.eu): Discovery/development Cosmeceutical Agents from Plant Biodiversity.
OLITEC (www.olitec.pharm.uoa.gr): public-private cooperation around olive trees science
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4. B. Natural products renaissance following European ban on antibiotics in feed
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Abstract
As the ban on antibiotics in feed approached (2006) many products (feed additives or feed ingredients) came to the market. Several were tested by independent research institutes. Interesting applications and innovations were developed. The position of natural products in farm management was discussed. Results of literature survey were published by Rikilt in the Natural Health series.

Introduction
Emerging problems with bacterial resistance against antibiotics have made EU governments critical about their use in feed. At the same time many feed additive producing companies went looking for alternatives for antibiotics and discovered several natural products that were active in a similar way. One would expect that the organic farmers would be in front of the natural product use but this is not the case (anymore). Homeopathy is sometimes used by them, but phytotherapy is rather unknown for them. Organic farmers had the impression that Wageningen University (WUR) was missing essential expertise on (or interest in) the subject (see also workshop 3B), so they turned to the NVF (Netherlands Assocation for Phytotherapy) veterinarians study group for help.

The Fyto-V project
Organic farmers in the Netherlands initiated the Fyto-V project (2006-2008) to increase the availability of herbals of proven quality and efficacy in feed, additives or animal medicine [1]. The NVF project group, coordinated by Maria Groot (Rikilt, WUR), had as additional members IEZ, two other private research institutes, specialised in phytomedicine (PhytoGeniX) and in organic agriculture (Louis Bolk Institute), the WUR department for animal research (ASG), the pharmacology department of the Veterinary Faculty,University Utrecht and a professional agricultural university (HAS).
IEZ started with an inventory that identified 142 herbal preparations available in 255 marketing formulas; mainly they were used as food additives for regular husbandry [2]. Based on the available literature data, and health problems the farmers mentioned, eleven products were selected for further clinical experiments. Three of them were products for pig (growth enhancers), three for dairy cows (aiming to help the immune system, in particular udder health) and five were products used for poultry against coccidiosis. First we did some *in vitro* quality tests of the products. They were checked for the presence of the claimed plants or compounds; the immune-enhancing, antioxidant and or bacteriocidal properties and the absence of contaminants (like growth hormones or synthetic medication). All eleven products stood these tests. As for the batch-to-batch consistency of the products, eight of the eleven stood the test and the remaining three did not have all the documents available to guarantee this consistency. All these testing also had a model character, both for producers (by reading the report they know how to make good quality products) as for the safety control institutes (as some herbs have oestrogenic or antimicrobial properties, it is necessary to devlop specific test procedures to avoid false-positive results).

DAIRY COWS
The products we tested in dairy cows were a garlic/stabilised allicin product; a yeast cellwandproduct enriched with selenium and a mixed herbs product that is popular amongst a group of Dutch dairy producers.
The products were administered, using a paired control design, in the autumn, when the cows were placed in the barn for the winter. Based on experiences in previous years we expected the cows to get an increased somatic cell count (SCC) and we hoped to see a difference in treated-non treated cows. Unfortunately in the year we dit the test the SCC was

not increased above normal level, so the only results we had here concerned safety, tolerability and acceptance of the products, and these were positive.

LAYING HENS
The tests on laying hens with coccidioses had to cope with other difficulties. Products were registered feed additives. Two were based on volatile oils and saponins (one from France, one from US), one was a mix of Indian (Ayurvedic) herbs sold as feed additive in Europe, one was a mix of garlic and cinnamon powder and again we had oregano-oil. We used a rather expensive validated (for animal medicine) challenge test model at WUR that was upto that moment only used for broilers. The WUR researchers claimed it could also serve for laying hens, but this was not the case. Allthough some of the five products that were tested appeared to have some effects on the infection, this was not significant. As also the positive control group (with monensin) gave no significant results we had to consier this test a failure. Particularly because we had asked the WUR to use an animal model (cq sufficient large numer of animals in the study) that reaches significance when a remedy shows about 50% of the effectivity that the chemical standard remedy has. So in this case again the products had good *in vitro* results that could not be supported by the *in vivo* trial.

PIGS
In pigs we investigated two feed additives containing (only, resp. mainly) essential oil of oregano, the third was a mixture of approximately 10 plant(extract)s. The products were used both on the WUR organic pig test farm and on two organic pig farms (by interested farmers). For each product approximately 64 organic pigs were fed herbal additives from weaning until slaughter; growers in four pens; fatteners in three pens. Control groups of the same size and housing received feed without these herbs. Study-parameters were growth, feed conversion, mortality, requirement of additional veterinary treatment, meat percentage, back-fat, carcass- and organ-findings. Liver biopsies were evaluated for parameters relating to pig health. In this case the herbal products showed positive effects on growth and/or feed conversion of weaner's as a trend ($p<0,12$). Although the weight difference was more than 10% with oregano, due to spread in results we could only conclude this being a trend. No negative side effects were seen. Slaughter data were promising (for example more meat, less fat) but not always consistent. To demonstrate health improvement, molecular parameters such as gen-expression for detoxifying enzymes (CYP450) were measured, in samples that were taken from the livers of the tested animals. Here all three products showed results. These gen-arrays appeared to be a not expensive, not invasive method that can give significant results related to *in vivo* tests and that is very promising [3].

Apart from these experiments we made an inventory of the bottlenecks in communication and legislation regarding herbal animal products. In workshop 4A these are discussed in detail. For organic farmers it is problematic that nowadays there are good herbal feed additives available for regular farmers, that the organic farmer may not use because no feed additives are allowed in EU directives for organic farming. For small producers selling herbal products to farmers it is problematic that if they sell an extract (like for example a tincture) they may only sell this as ingredients to feed companies, not to farmers directly.

Output for farmers in stable books.
After finishing the Fyto-V report the government funded more fundamental research into the possibility of plant compounds (not herbs) replacing antibiotics. As no pharmaceutical company will go this way (known as plant compounds, the high costs for the registration process will not be covered by the profits when selling these as medicines) this was a waste of money, and also a waste of expertise as the Fyto-V group was not welcome to participate in this research.
In the same period (2009) organic farmers wanted to have more easy access to the results of the literature studies done in the Fyto-V project and their main question was: what can we do on our own farm?

Therefore in a cooperative project Rikilt and IEZ produced stable books [4], based on the literature database that was created during the Fyto-V project and the expertise of several vets and scientists in the NVF veterinary study group. We tried to write it understandable and topic-related (life cycle period or diseases were both used) for the farmers. We included some farmer's experiences and added the list of producers of the natural products. In an addendum students of the veterinary faculty supervised by Rikilt made analyses of the scientific literature available on the products mentioned in the books. This of course was not so much of interest to the farmer, but it can be very important to help him discuss the (wish to) use of these products, that are still unknown to most vets. These parts are only available in Dutch; they were left out in the translation.

In the stable books the importance of preventive use of herbs is emphasized. This should be a part of an active health-promoting management. Such an approach requires early identification of problems in animals. Timely correction of small problems by supplying natural products in feed or water, can prevent the necessity of heavier medication down the line. Most herbs, and more so herb mixes, can be used for a multi-functional approach for health improvement and for improved feed uptake. These two can often not be separated. It is all about fine-tuning. Acute and severe cases require veterinary assistance and drastic remedies. But this should only be the small top of a pyramid; the farmer is responsible for a firm basis in sound management.

An example from the poultry book. Chapter 2: *Respiratory system* distinguishes just two types of problems : Sniffing, coughing and breathing difficulties; and Infectious diseases (virus, bacteria, fungi). In the first case the important management points that are given are: proper ventilation for enough oxygen and pathogen amount reduction; dust reduction (eventually temporary use of sprays); vaccination; use of natural products to reduce the vaccination-reaction, increase resistance and restore mucous membranes. These measures are also important in case of infectious diseases, but because these can spread so rapidly it is important to act quicker. The natural products that are on the market are mentioned (Sprays with *Eucalyptus, Mentha,* or *Melissa oil;* Indian herbs products; products with *Echinacea,* garlic and oregano oil), and also some attention is paid to traditional products that easily can be acquired by farmers or cultivated on the farm (blackseed, elderberry, nettle).

Examples from the pig book: This book starts with the cornerstones of healthy pig husbandry which are: housing, feed, light, air, space and rest. Pigs are very susceptible to stress. Critical moments are discussed: birth, weaning, feed changes, caretaker changes, medical interventions. After discussing the possible use of natural products for intestinal problems, claw health, worms and skin parasites, follows a chapter about hygiene products. At this moment the use of products with *Bacillus subtilis* (probiotics) for cleaning stables is getting very popular in Europe.

An interesting follow up on the stable books is that a group of (regular) pig farmers used them to make their own feed mix and they now offer to the public their "herb pig meat”: it tastes good (sells good!) and they don't need to use antibiotics anymore because there are several health advantages related to this herb feeding.

Thanks to a small grant the stable books were translated in English. That is very important for us, because it gives us the possibility to discuss the here chosen approach with vets and farmers in other countries.

It is a pity that no further financial support for the Fyto-v website was generated; IEZ and Maria Groot (Rikilt) created it and we had many positive responses, but needs to be modernised with more actual literature references. Students from the agricultural professional university in Den Bosch are taking this up now.

Discussion: herbs as a part of a general holistic approach in animal health care
The NVF, Netherlands Association of Phytotherapy, has started an innovative project with 13 SMC's (small or medium sized companies) that aims at banning the use of antibiotics in a number of regular pig and cattle farms. Herbal products are only a small aspect of this project; even more important are bacteria (*Bacillus subtilis* mainly) that are being used for the stables and for the farmers and their coworkers. The general idea is, like in the stable books, that management is the most important issue. We try to give the use of natural products a place in the daily practice of the farmer. Not as a replacement for the veterinary's intervention with chemical/synthesized medicine, but as a prevention method that aims to to avoid as much as possible the more drastic chemicals. This is different from the way the government sees it (and WUR has often tested it): they hope to replace synthetic antibiotics by herbal products or even by isolated phytochemicals without altering the whole management. In our opinion this is not the optimal way to use herbal products. That is why we included in our projects many general management improvements, for example water systems that are hygienic and warn immediately the farmer if less water is used; air improving systems, etcetera. We hear from several of the participating companies that it is rather difficult to change the Dutch authorities' views, whereas abroad (for example Germany, England) at least the local authorities are more flexible and cooperative.

The position of WUR with its expensive standard test models and output to government and governmental institutions has to be taken in concern here.
To our experience we see, when testing herbs in both animals and humans, that they do often perform in the validated test models with an effect in between the two controls (those being: no medicine and the normally used chemical medicine). So for better research the standard test models have to be enlarged or complemented by other tests, like the DNA micro-arrays I mentioned before.

Although I contributed to the text book of Katerere/Luseba [5] I think the book of Wynn/Fougere [6] is a more practical step forwards for vets. We use this book as the introduction book in the phytotherapy course that the IEZ organizes for vets. The holistic approach, still combined with sound scientific background, suits better our aim at multi-target problem solutions.
Veterinary practices with companion animals give better opportunities for an individual tailor-made prescriptions of herbs; this may be too costly for most farm animals.

I would very much like to hear if you have in your country (the same, or other) experiences with this approach; or if you would prefer another approach to the use of herbs.

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