

Internet marketing of the herbal product ginger for use against nausea and vomiting of pregnancy



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Abstract

Aim: The purpose of the study was to evaluate Internet marketing of ginger for use against nausea and vomiting during pregnancy (NVP) with particular focus on claims related to safety and efficacy in this indication.

Method: A systematic study on the Internet using the terms “*pregnant and nausea*”, “*pregnancy and nausea*”, “*pregnancy and morning sickness*” and “*morning sickness*” was performed on September 14th and 15th and October 26th 2009. The search engines www.google.com and www.yahoo.com were used for all searches. Web sites containing information about NVP and suggested one or more treatment were included.

Recommendations of ginger that were included were ginger powder, capsules and root. Sites recommending ginger cookies, candies and similar products were excluded.

Ginger retail sites were located using the terms “*ginger*”, “*buy ginger*”, “*purchase ginger*” and “*sale ginger*” on September 24th 2009. Sites considered relevant were those where ginger products could be purchased directly or by clicking on provided links. On December 17th 2009 the term “*safety and ginger and pregnancy*” was used to gather sites where the safety of ginger in pregnancy was the main topic. Statements on the effectiveness against NVP were also investigated.

Results: A total of 255 Web sites were examined in the study. Of these, 88 unique sites fulfilled the criteria's for further study. Ginger was recommended on 30 (61.2 %) of the 54 relevant NVP treatment sites. The majority of sites were commercial. Generally, the information given regarding safety of ginger during pregnancy was scarce and when such information was provided the recommendations varied. “*Nausea*” was given as indication for use on 10 (55.6%) of the 18 ginger retail sites whilst five (27.8%) mentioned “*morning sickness*” or similar. One site stated that ginger product was not to be used during pregnancy and lactation unless a healthcare practitioner had directed it. Another site said it was safe for short term use during pregnancy. The others neglected to give any such information. Six Web sites of scientific interest and 11 sites aiming at the common consumer were found in the ginger safety search. Nine (52.9%) of these 17 sites found that ginger could be used safely by pregnant women.

Conclusions: Ginger is frequently recommended on the Internet as a remedy for NVP, but limited information is provided about the safety of ginger in pregnancy unless the word safety is included in the search term. When this is done, the majority of sites state that ginger is effective and safe for use against nausea and vomiting during pregnancy.

List of abbreviations and definitions

NVP	nausea and vomiting in pregnancy
CAM	complementary and alternative medicine
NHP	natural health products
HG	hyperemesis gravidarum
Internet domain	the unique name, brand of an organisation, person etc., e.g. www.babycenter.com , also called the home page, start page
Web site	a document or resource of information available on the Internet. A Internet domain can have numerous of these, e.g. http://www.babycenter.com/0_morning-sickness-causes-concerns-treatments_254.bc
Sponsored Web site	A Web site that pays a search engine in order to appear every time certain terms and keywords are entered into the search engines' browser
Retail Web site	A Web site where it is possible to make online purchases
Non retail Web site	A Web site providing information, services etc.
Chinese proprietary product	Traditional, Chinese medicine containing either plants, animal parts or minerals in standardized amounts and formulations

1. Introduction

1.1 The use of the Internet as a health information source

For many people, using the Internet to retrieve various information or entertainment is an everyday procedure. Studies have found that health related Internet searches are common. An October 2006 report from The Pew Internet & American Life project states that 80 % of all American Internet users have used the Internet for health related searches (1). Amongst the other findings from this study was that women are more likely to look for health information than men, and that of the total 80 %, 27 % had been searching for information related to alternative treatments or medicines, whilst 64 % had been looking for a certain condition or medical problem.

How the actual search is performed will vary for every individual, but some “methods” seem to be more common than others.

In the Pew study it was reported that 66 % of those who had searched for health related information on the Internet had begun the search at a search engine the last time they had performed such searches. Some chose to start at a Web site that was health related (27 %) (1). One study tried to find out both how the Internet search is performed and how the credibility of retrieved information is validated. The study sample was small, with only 21 individuals in focus groups, and 17 performing given tasks and interviewed afterwards. The 17 individuals were each given eight or nine questions (no mention of why this varied), and had 20 minutes on each question. The chosen starting point for all but two questions were search engines. 97.2 % of all the links that were investigated were amongst the 10 first search results (2). In both this and in a study that found the Internet to be third most important information source on pregnancy and delivery (3), the vast majority turned to search engines and one can assume that this is the preferred method for most people. As mentioned, the study with focus group interviews and task performing also tried to find out how the participants appraised the information found. Interestingly, there was a difference between what the focus groups said they would like the information site to be, in order to check the information credibility, and what the volunteers in the practical experiment did. Ideally, the source of information should have some sort of authority, e.g. a governmental or scientific institution, professional but yet

understandably written, and the use of references, preferably scientific. In reality, the volunteers did not bother to check where the information came from, nor read disclaimers or the “about us” information that most sites provide (2).

Yet another study confirms these findings; participants in focus groups that were given tasks to answer (n = 46), used search engines when information was sought, and had opinions on what makes a site trustworthy but could not justify/remember why they had chosen to use the information of a Web site after the tasks had been completed (4). Also here, it was most common to investigate sites on the first results page.

Today’s most popular Internet search engines are Google and Yahoo (5;6). It has been reported that the searchers geographical whereabouts affect what sites that are shown on the result page, as can the browser features and the Internet service provider (7). Also, search engines differ in how they arrange the result pages.

Different tools and methods have been applied when the reliability of Web sites has been investigated; one such is the DISCERN instrument. This tool is used on health information sites with treatment choices, and consists of 16 questions to the reader about the Web site investigated. A site will ideally state the sources of information (references), provide a published/last updated date, be balanced and unbiased and state both benefits and risks of i.e. a treatment (8). A study with 57 participants attending workshops where a Web site providing information on breast cancer treatments was investigated using the DISCERN instrument gave promising results. The participants were a heterogeneous group, both professional and consumers attended. Prior to the workshops, 41 % had used different criteria’s for quality of online information. Afterwards 89.6% reported a change in their appraisal of consumer health information; becoming more systematic and critical was common. It was found that 96.2% of the participants saw the DISCERN instrument as helpful when discriminating between online information treatment sites of high- and low-quality (9).

1.1.1 Pregnant women and their use of the Internet

Research has also been aimed at certain groups, e.g. if and how pregnant women use the Internet. Of 182 pregnant Swedish women participating in a study from 2005, 84 % had used the Internet to retrieve information about their “condition”. It seemed most common to search for foetal growth and development information. (10) Most of the women considered the

information to be reliable (exact percentage value was not given), and did not discuss the information with their midwife. A recent study from 2009 where 303 midwives from different countries took part, found that 67 % of them thought that the information pregnant women found on the Internet had an impact on the managing of the women's pregnancy (11). In this study, 86 % of midwives had experienced discussing with a pregnant woman the information she had found, as a contrast to the Swedish study where the dialogue did not seem to be quite as open.

In an American study from 2006, it was found that the Internet was the third most important source of information about pregnancy and delivery, ranking almost equal to doctors. (Books, family and friends were perceived as most important. Percentages were not given) (3).

1.2 Herbal products

Historically, herbs have been widely used in "*traditional medicine*", and even today, in some countries in Asia and Africa, 80 % of the population relies on traditional medicine in the primary health care. Financially, herbs are the most lucrative part of traditional medicine. Western Europe revenues in 2003-2004 were US\$ 5 billion, for Brazil the sum was US\$ 160 million. In China, where herbal products use is common, sales of such products in 2005 was US\$ 14 billion (12).

Different studies report different percentages on how common it is to use herbal products. Table 1.2.1 shows a few results from studies in different regions of the world.

Table 1.2.1 Some studies from four English speaking countries showing the use of herbal products (13-17)

Country	Study	n	% used herbal products for the past 12 months
UK	<i>Thomas, K.J. et al 2001</i> ¹⁴	2645	19,8
USA	<i>Tindle, H.A. et al 2005</i> ¹³	31 044	18,6
	<i>Rafferty, A.P. et al 2002</i> ¹⁶	3 764	20,5
Canada	<i>Singh, S.R. et al 2006</i> ¹⁷	11 424	9,3*
Australia	<i>Zhang, A.L. et al 2008</i> ¹⁵	2526	22,6

*:use over the past 2 days

Pregnant women's use of herbal products has also been investigated. In chapter 1.7.2 some of the studies that have dealt with this subject are presented.

1.3 The use of the Internet for shopping herbal products

The marketing of herbal products on the Internet is common (18), but an estimation of how common online herbal shopping is, is difficult to find any data on.

The Norwegian Medicines Agency reported that in a survey amongst 500 Internet shoppers, 276 of these (55.2 %) had bought or considered to buy "*natural products*" online. Herbal products ranked as no. 1 amongst the natural products purchase categories (55 %). Pricing and the product not being available in stores were the main reasons for purchasing or considering purchasing products online (47 and 34 %). One percent reported that their doctor had recommended them to purchase a specific product online (n ≈ 3) (19).

Internet/mail order counted for 7 % of the total natural product sale in Norway, 2006 (20).

In a report it was found that 8.6 % of Internet shoppers in Canada had bought something from the rather unspecific category "*other health products, beauty and vitamins*" in 2007 (21). There were 26 588 participants in this survey (22).

Of the American Internet users, 39 % had purchased items via the Internet according to a 2002 investigation (23). Specific data on herbal products purchase was not available.

Why people uses the Internet for purchasing was not investigated in these studies, but the opportunity to make quick price comparisons, the fact that it can be performed at any time of the day; it is convenient and easy, all this might be the reason why people turn to this.

Recently it has been documented that a “*purely plant based (herbal)*” product sold on the Internet, marketed as a slimming product, in fact contained sibutramine, a substance that is not a herb but under prescription regulation.(24). It has been used as an anti-obesity agent, but due to a risk for developing stroke and myocardial infarction amongst others, the European Medicines Agency (EMA) recommended that sibutramine preparations/medicines should be removed from the European market in January 2010. The benefits from these medicines did not outweigh the risk of adverse effects (25). The US Food and Drug Administration (FDA) currently only disapprove the use of sibutramine medicines by people that have a history of cardiovascular disease (26).

Clearly there is a risk for unintentionally consuming sibutramine in “herbal” products for people in general and also those in risk groups.

Reports of other herbal products being contaminated or containing medicines are also present. A systematic review from 2002 found 22 articles with this topic, and a wide range of medicines had been added to different herbal products (27). Some mentioned in that review and others found are given below.

Digitalis lanata Ehrh was found in a botanical dietary supplement after a case report of a woman being admitted to hospital with a serum digitoxin level that was toxic (28).

A Chinese herbal product used to aid back pain and arthritis by four people was shown to contain aminopyrine and phenylbutazone. These substances are known to cause agranulocytosis, which was the indication of hospital admittance for the four cases (29).

Corticosteroids have been found in herbal creams used for atopic eczema in the UK (30). The anticonvulsants phenytoin, valproate and carbamazepine were found in a Chinese proprietary product, although they were not amongst the official constituents of the product (31).

1.4 Internet marketing of herbal products

Investigation of the Internet marketing of the eight most sold herbal products in the US showed that 55 % of the retail sites “claimed to treat, prevent, diagnose or cure specific diseases” (32).

It has been found that Internet marketing of herbal products containing saw palmetto or cranberries aimed at prostate hyperplasia and urinary tract infection on Norwegian Web sites had a large proportion of health- and medical statements. Thirty-three out of 79 Internet advertises (42 %) had one or more illegal health claims. Stating that “*no side effects will occur if the daily recommended dosage is used*” or that “*extensive study has proven its high efficacy against urinary tract sufferings*” was given as examples of this. Claims that according to Norwegian legislation are illegal were only found on the Internet advertises and in advertises from health food stores. Advertises from pharmacies and magazines did not present such illegal claims (33).

Previous studies on CAM, complementary and alternative medicine Internet advices for several different diagnosis and problems have shown that in many cases the information and/or the advices are erroneous and sometimes even dangerous. A few are presented here.

A recent study investigated Internet NHP, natural health products, for postmenopausal osteoporosis treatment on 38 different Web sites. It was found that many of these sites (reportedly 82 % and up) contained information about both evidence based and non evidence based CAM (34). It becomes difficult for the consumers to know what sites to trust. Not giving references that could support the information was considered a problem; is the information reliable or not?

Some Web sites claim that there are herbal products that can cure cancer. In a study of Web sites with herbal treatments for cancer it was found that many of these claimed that different herbs could prevent, cure or treat cancer. The sites were divided into “*commercial*” and “*non commercial sites*”, and of the non commercial sites (n=34) 58 % of these had “*cancer cure*” as a claim or statement, and 89 % also had “*cancer treatment*”. For the non commercial sites the percentages were 1 and 30 (35).

From these findings it can be derived that scepticism should always be applied when browsing the Internet, perhaps especially when encountering information on commercial sites. The fact that mentioning potential adverse effects or contraindications is often neglected is

also disturbing. The Food and Drug Administration prohibited the sale of dietary supplements containing ephedra in 2004 (36). The year before, an article presenting results from an evaluation of Internet marketing of such products was published (37). It was reported that one of the 32 Web sites investigated had recommended a product containing ephedra for patients suffering from hypertension and coronary disease, despite the fact that a raise in blood pressure and inducing tachycardia had been reported as adverse effects for ephedra products (38). Even stroke and cardiac arrest has been reported (39), and also psychiatric symptoms (38). The fact that such an ill advice was given on one of the Web sites should be a warning for both regulatory agencies/boards and consumers seeking information on the Internet.

1.5 Nausea and vomiting during pregnancy

Experiencing nausea and vomiting (NVP), often referred to as “*morning sickness*” is the most common GI-tract problem for pregnant women (40). It is estimated that between 50 and 80 % of pregnant women suffer from this, most often during the first trimester (41;42). Typically it appears in the fourth week after the last menstruation cycle, peaks in week nine and diminishes by week 12. It harms neither the mother nor the baby in most cases (43).

First line treatment is taking some practical measurements. Resting, avoiding certain foods, frequently eating small meals rich in carbohydrates and reassurance that NVP is common and not harmful is sufficient for some (44). Few countries have licensed drugs with nausea and vomiting during pregnancy as an indication. In USA and Canada, a combination of the antihistamine *doxylamine* and *pyridoxine* (vitamin B₆) is used for this indication (43). In a Cochrane review the conclusion was that vitamin B₆, and most of the antihistamines and phenothiazines were helpful. The evidence on ginger was promising, acupuncture/acupressure results mixed (45).

Hyperemesis gravidarum (HG), severe vomiting, is a condition that affects 1-5 % of all pregnant women. This can lead to hospitalization due to fluid,-electrolyte- and nutrition imbalance (43).

1.6 Ginger

Zingiber officinale Roscoe, commonly known as ginger, has been used both as food flavouring and for medical purposes for centuries. Ginger is a plant in the “ginger family”, *Zingiberaceae*, which is the same family as cardamom, and is found in Asian countries such as India and China, but also in other tropical areas such as Jamaica.

It is the rhizome of the plant that is being used; either freshly cut, or dried and ground into powder (46).



Figure 1.6.1

Fresh ginger root

Ginger contains numerous constituents, and these may vary between fresh and dried ginger, and where it has grown. Starch is the major constituent, up to 50% of ginger is starch (47). The gingerols family has been found to be a major constituent (48). Using gas chromatography and mass spectrometry, it was found that the percentage sample composition of (6)-Gingerol in two different fresh ginger samples was between 27 and 34%. Shogaols, dehydrated products of gingerols are also found, and it is the gingerols and shogaols that make ginger so pungent (49). One study found 115 compounds in commercially processed dry ginger (50), of which 45 had previously been found by the same group in fresh ginger (49).

Higher levels of shogaols and lower levels of gingerols were found in the dried ginger compared to the fresh. This seems logic as shogaols are dehydrated gingerol products (50).

Ginger has been applied for various conditions, such as nausea, colic, flatulence, cough, anorexia, arthritis, cholera, baldness and many more. It has been used fresh or dried, e.g. fresh ginger is taken orally for baldness and dried ginger (also orally) for stomach pain (46).

Today, arthritis and treating and preventing nausea are the conditions perceived as the most relevant and interesting to treat with ginger compounds (47).

Many different compounds of ginger have been identified; however, the active ingredient(s) and exact mechanism of action against nausea and vomiting have not been clarified. It is therefore possible that preparations may differ in their effect on NVP due to the origin of the ginger and the manufacturing procedure. This was found in a study where different ginger products were examined using HPLC; there were notable differences in the compositions (51).

1.6.1 Effectiveness against morning sickness and safety

In a small, double blind, placebo-controlled, randomized study with 13 women in the test group and 10 women in the control group, it was found that 77 % of the pregnant women treated with a tablespoon ginger syrup containing 250 mg ginger four times daily had a positive effect on nausea, whilst only 20 % of the women receiving placebo had an equal improvement. They also found that 67 % of the women receiving ginger and 20 % of the placebo group had stopped vomiting by day 6 of the treatment. The results were not statistically significant (52).

Another double blind, randomized study compared the effect of ginger and vitamin B₆ on NVP. There were 35 women receiving ginger, and 34 receiving vitamin B₆. Eighty-three percent in the ginger group had an improvement in the nausea symptoms, and 68 % of the women receiving vitamin B₆ also had an improvement. The ginger group had a significantly greater reduction in nausea ($p < 0.024$), but regarding vomiting no significant difference was reported. The ginger group took 500 mg ginger twice daily (53).

Almost half of the pregnant women in one study did not find ginger helpful in treating NVP (54). A possible explanation for this could be the fact that the women in this study had ingested ginger in different forms; anything from ginger capsules, ginger tea, ginger cookies, and ginger candy to inhaled powdered ginger, and so comparison of effect is difficult due to different amounts of the active components of ginger and other substances such as i.e. sugar. A connection between low blood sugar and NVP has been found, and so nibbling on ginger cookies or candies can alleviate the NVP- not because of the ginger but because of the sugar in candies and cookies that raise the blood sugar level (55).

Table 1.6.1.1 shows some other studies where the efficacy of ginger products against nausea and vomiting has been investigated.

Table 1.6.1.1 Some studies that have reported on the efficacy of ginger against nausea and vomiting/hyperemesis gravidarum (52;53;56-59)

Study	Dose and duration	Study sample	Safety concerns	Efficacy
<i>Fischer-Rasmussen et al 1990</i> ⁵⁶	Four days treatment with 1 g dried rhizome a day	30	None found	Statistical significant decrease in nausea for the ginger group compared to the women receiving placebo
<i>Vutyavanich et al 2001</i> ⁵⁷	Four days treatment with 1 g dried rhizome a day	32 test:38 controls	None found	More effective than placebo against NVP
<i>Keating and Chez 2002</i> ⁵²	Two weeks treatment with 1 g dried rhizome a day	14 test:12 controls	None significant found	May be useful against nausea and vomiting
<i>Sripramote and Lekhyananda 2003</i> ⁵⁸	Three days treatment with 1.5 g dried rhizome	64 test:64 controls	None significant found	Ginger and vitamine B6 are equally efficient against nausea and vomiting
<i>Smith et al 2004</i> ⁵⁹	Three weeks treatment with 1050 mg a day	146 test:145 controls	None found	Ginger and vitamine B6 are equally efficient against nausea and vomiting
<i>Ensiyeh and Sakineh 2008</i> ⁵³	Four days treatment with 0.5 g twice daily	35 test:35 controls	None found	Significantly greater effect than vitamine B6

In general, it seems to be likely that ginger is effective against morning sickness.

It is believed that the effect of ginger on nausea and vomiting is most likely caused by a local action on the GI-tract (47).

A prospective and comparative study did not find any significant increase in major malformations in newborns due to the use of ginger. The only statistically significant difference in outcome was that the newborns of ginger-using mothers tended to be heavier than the newborns in the control group (54).

The disadvantage when assessing the safety of ginger during pregnancy is that many of the trials have been performed with few participants.

A study where 5 g dried ginger was given twice daily, and where the subjects had a diet with high amounts of fat found that ginger inhibited platelet aggregation (60). Therefore, a possible interaction between ginger and warfarin has been suggested. However, another study found

that 4 g powdered ginger daily for 4 months did not affect platelet aggregation, nor the fibrinolytic activity or levels of fibrinogen (61). The same study found that a single dose of 10 g. ginger did inhibit platelet aggregation (61). A more recent investigation on ginger and its possible effect on warfarin did not find a significant inhibition on platelet aggregation or effect on the pharmacodynamics and pharmacokinetics of warfarin (51). The ginger dose was 3.6 g. daily, for 5 days. This is well above the recommended daily ginger intake for aiding morning sickness. Also animal studies have found that ginger did not have an effect on platelet aggregation (62).

A conclusion derived from this will be that a pregnant woman on warfarin should be under close observation from her doctor if she starts using ginger, just to be on the safe side.

Rat studies have not found ginger to be a teratogen (63;64). One did however find larger foetuses in the rats given ginger, which is consistent with the results from the human prospective study (54), and a significantly higher rate of early embryo loss.(63)

A suggestion that ginger affects testosterone metabolism in foetuses(65) has not been proven.(66)

Daily dose recommendation is normally around 1 gram, as this has been used safely in many of the studies.(52;53;57;59)

1.6.2 Use of ginger against NVP

Three studies focusing on the use of herbal products against NVP have been found (67-69).

Ginger, acupuncture and vitamin B₆ were the most popular CAM in a study from the Motherisk Nausea and Vomiting Helpline (50.7, 45.8, 29.2 %) (67). In one study with 20 women experiencing NVP, 10 out of these chose a herbal product to treat the condition. Six of the ten chose ginger tea (68).

It was also found that the women used CAM because they did not want to use medications unnecessary, and feared of harming the foetus (67). This perception of medications being harmful to the unborn is common, and it has been found that most women overestimates the teratogenicity risk from medications.(70) Another study from Motherisk found that even though women were told that a medication with a combination of doxylamine and pyridoxine

was safe to use against NVP, only 39 of 59 respondents later on reported using this. The women did not find the evidence on its safety to be sufficient (69). It was found that 11.9 % of the pregnant women preferred to use only ginger to treat NVP (69).

When the use of herbals independent of indication is investigated, the reported prevalence of ginger use by pregnant women differs greatly. This is shown in table 1.6.2.1, where the percentages of ginger use ranges from 0.6 to 47 amongst the herbal product users.

Table 1.6.2.1 Studies that has investigated the use of herbal products during pregnancy (68;71-79)

Study	Country	Study sample	Use of herbal products during pregnancy(%)	Use of ginger by the women using herbs(%)
<i>Nordeng, H. et al 2004</i> ⁷¹	Norway	400 3 days-postpartum women	36	10,4
<i>Holst, L. et al 2008</i> ⁷²	Sweden	860 215 women up to 12 weeks pregnant	0,9	0,6
<i>Holst, L. et al 2009</i> ⁷³	UK	578 pregnant women 20 weeks and more	57,8	47
<i>Maats, F.H. and Crowther, C.A. 2002</i> ⁷⁴	Australia	211 pregnant women 26 weeks and more	Not given	20*
<i>Pinn, G and Pallett, L. 2002</i> ⁷⁵	Australia	305 women between 16-24 weeks pregnant	12	0,8
<i>Forster, D.A. et al 2006</i> ⁷⁶	Australia	588 women around 36-38 weeks pregnant	36	12
<i>Tsui, B. et al 2001</i> ⁷⁷	USA	150 pregnant women	13	6,7
<i>Glover, D.D. et al 2003</i> ⁷⁸	USA	578 pregnant women	45,2	0,9
<i>Moussally, K. et al 2009</i> ⁷⁹	Canada	3354 women	9	3,5
<i>Westfall, R.E., 2004</i> ⁶⁸	Canada	27 pregnant women	96 (n=26)	22.2 (n=6)

*: During the first trimester

1.7 Distribution of natural health products by retail pharmacies

Many pharmacies are increasing their natural health product assortment, and herbal products are amongst these. This has been criticised by some that feel the pharmacy should not sell products for which the certain mechanism of action, effect and/or safety data is not established (80). However, it might not be a bad idea that the pharmacy distributes these products when studies of the advices given by health store staff show that the quality of advices could be higher (79-82).

In one study, “*medical herbalists*” were located via searches using Internet search engines and emailed. They were asked about the use of three herbs, amongst these ginger, and if it was safe for a pregnant woman to take these for morning sickness. Ginger was recommended by 19 (45 %) of the herbalists, and nine of them failed to mention any side effects (81).

Another study investigated the advices given on morning sickness and migraine during pregnancy. One hundred and fifty five health stores in Phoenix, USA were phoned by an “*8 week pregnant woman*” asking about morning sickness and migraine treatments. The answers given were compared with the evidence based knowledge currently available (September 2004). Ginger was the most mentioned morning sickness treatment mentioned. It was also found that five percent of the advices given were for products that are contraindicated in pregnancy, and dosage and duration claims were often wrong (82). Advices given by staff on 34 health stores on breast cancer have also been investigated. Eight (23.5%) mentioned that there could be a potential interaction with prescription drugs, and one recommended to discontinue Tamoxifen. Two suggested that breast cancer could be cured by products from the health store (83).

Pharmacies and health stores have also been compared; staffs have been asked about NHP treatment of hypertension. Seventy percent of the health store staff stated that NHP were superior or equally effective as prescription medicines for hypertension treatment and all (n=20) recommended NHP. Only four of 38 pharmacists suggested NHP (84).

From the latter study it seems that pharmacies can be considered to be more neutral and wanting to have documentation on effect and safety before making a recommendation than health store staff. Also, one can encounter potentially dangerous advices in health stores such as recommending discontinuing of Tamoxifen to a breast cancer patient. Pharmacies are trusted by the public, and people believe that the advices given there is for their own good (85). Pharmacists must know where to find appropriate information on herbal products so that they can guide pregnant women and the public in general to the correct decisions. It is known

that the Internet is an increasingly important information source for people (1), and the lack of quality assurance of the information there should be mentioned if discussing such information with patients.

2. Aim

The aim of this study was to:

1. Identify if ginger is being suggested as a treatment for nausea and vomiting during pregnancy on Web sites written in English
2. Study the marketing of ginger with respect to
 - claims about safety and efficacy, and use in pregnancy
3. To get an impression of the reliability of the Web sites found:
 - is there a difference between retail and non retail Web sites

3. Method

This study is composed of three separate Internet information searches.

First, Internet searches to detect what treatment suggestions for NVP the sites gave were performed. After establishing that ginger is frequently recommended for NVP, an attempt to find Internet ginger retail sites was performed. This was then followed by a search investigating statements about ginger use during pregnancy and its safety and efficacy against NVP.

Only when ginger root, ginger powder or ginger capsules have been mentioned has it been recorded as relevant. Ginger candies, cookies and similar have not been included in this study. Because these products have varying ginger content and often have a high sugar content, a positive effect on the NVP could just as easily be caused by a raise in blood sugar level (55). Recommending such products is in reality a recommendation of making dietary changes; frequent snacking of cookies or candies to avoid low blood sugar levels.

After some consideration it was found that the small sample size made statistical analysis irrelevant.

The two search engines www.google.com and www.yahoo.com were used for all searches in this study. These were selected on the basis of their popularity (5;6). A total of 255 Web sites have been found and investigated during this study.

3.1 Internet-suggested NVP-treatments

The four first terms in figure 3.1.1 were entered into the two search engines on September 14th and 15th 2009, while the fifth was entered on October 26th 2009. The reason for this time difference was simply that it was forgotten to include the term into the initial search.

- Pregnant and nausea
- Pregnancy and nausea
- Pregnant and morning sickness
- Pregnancy and morning sickness
- Morning sickness

Figure 3.1.1: The five search terms entered into Google and Yahoo in order to investigate treatment advice on NVP

Each Web site link on the first result page was investigated, and the opening site (the one that appeared when clicking on the link) was printed for archiving. Where relevant, other pages were also examined for further information gathering, i.e. when the rest of the article was on page two.

The Web sites were categorized as either sponsored, retail or non retail sites. Sponsored sites appeared on the top, bottom or right side of the results pages under a banner saying “*Sponsored Results*”. Retail sites provided purchase opportunities, non retail sites did not.

The number of sponsored sites was noted, and duplicates between the two search engines within one search term, and overall duplicates were accounted for. A web site was categorized as relevant if it contained information about NVP, and suggested one or more treatments. The treatment suggestions were recorded for each relevant site.

Sponsored sites and non sponsored sites were investigated separately. The reason for this was to see if there were differences in their features, but also that it is uncertain if consumers would rely on the information provided by sponsored sites. A review article found that people

avoid Web sites that are transparent commercial(86), and sponsored sites must be said to belong to this group.

Suggested nausea aids were categorized in 5 different categories; these being

1. ***Dietary/practical advices***, such as nibbling, getting up slowly from bed, what kind of food to eat and so on.
2. ***Ginger***, in different forms, i.e. root, powder, capsules. (Ginger ale, ginger biscuits and so on are not included in this study)
3. ***Acupressure***, either acupressure in general or, as most sites add, wristbands often referred to as “seasickness bands”
4. ***Vitamin B₆***, mentioned specifically. If mentioned as a combination with medications; not recorded.
5. ***Prescription medicines***, when the site mentions different brands, active ingredients or has links to “anti nausea medicines” or similar

Other features recorded:

- If the site was retail or not. A site was considered as retail also if it contained links to retail sites.
- Whether or not the published information had a published date and/or an updated date.
- Use of references.
- If the name of the author(s) was given
- If the profession of the author(s) was given, and if it could be perceived as health personnel by lay people. Professions included in this category were i.e. occupational/alternative therapist, doctors and nurses.

Alternative therapists may be perceived as trustable sources, much like doctors and other health care personnel by some people, and are therefore included in the somewhat misleading “*health personnel*” category.

In some cases it was found that although the authors were not identified, the “*about us*” feature listed the names and occupations of the contributors to the site. These were classified as health personnel written if the occupations were relevant.

The domain endings of the sites were also recorded.

Differences between Google and Yahoo results, and differences between retail sites, non retail sites and sponsored sites were then compared.

3.1.2 An Australian identical Internet search was performed

These five search terms were also typed into www.google.com and www.yahoo.com by a person localized in Australia, between the 3rd and 8th of February 2010.

The only feature of the Australian results that were investigated was the domain endings.

3.2 Ginger retail sites

On September 24th 2009 a search using Google was performed. On September 28th 2009 the same searches were conducted using Yahoo. The search terms used are given in figure 3.2.1.

- *Ginger*
- *Buy ginger*
- *Purchase ginger*
- *Sale ginger*

Figure 3.2.1 The four search terms used to find retail sites that sold ginger

A site was categorized as relevant if it was possible to purchase ginger products (not food related such as ginger ale, biscuits and so on) directly or by clicking on links provided by the site. Wholesale sites were excluded since these would not be relevant for a consumer.

Duplicates of the sites were accounted for.

Sponsored and non sponsored results were investigated together, as the aim was to study retail sites.

The sites that were found relevant, were then investigated regarding their

- site nationality
- health claims about ginger on NVP
- health claims about ginger on nausea in general

Due to a small sample size, there was no comparison of Google and Yahoo results; only an aggregated result was presented.

3.3 The efficacy and safety of ginger

On December 17th 2009, a search was conducted at www.google.com and www.yahoo.com , using the following phrase as search term: “*safety and ginger and pregnancy*”.

The first result page of both search engines was printed, as were each of the individual results. The main feature investigated was the provided information about effect and safety. Also the use of references, a named author and nationality of the site was noted. A web site was categorized as relevant if it contained information about ginger and safety during pregnancy, effectiveness against NVP or both.

The results were divided into two categories:

1. **Scientific sites.** If the provider of information was not aiming for the common consumer.
2. **Health information sites.** These were sites marketed towards the common man browsing for NVP treatment alternatives.

This was done in order to see if the safety and effectiveness concerns have been addressed in the common health/herbal information on the Internet, and also to identify potential differences in safety and efficacy opinions between the two categories. It was also considered interesting to see the nature of the results provided through these information channels; would perhaps one of the categories appear more often than the other?

4. Results

4.1 Results from the treatment suggestions search

Table 4.1.1 shows the individual search results for Google and Yahoo separately, and also the total amount of unique Web sites found. Duplicates have been removed so that it is not the suggestions from each and every site that has been recorded, but the suggestions from every unique site.

Table 4.1.1 The search results for Google, Yahoo, both together and the number of unique sites when duplicates have been excluded

Search terms	Google	Yahoo	Total	Unique sites (n/N)
<i>"Morning sickness"</i>				
Non sponsored Internet sites	11	10	21	13/21
Sponsored Internet sites	4	8	12	6/12
<i>"Pregnant and nausea"</i>				
Non sponsored Internet sites	10	10	20	15/20
Sponsored Internet sites	1	1	2	1/2
<i>"Pregnant and morning sickness"</i>				
Non sponsored Internet sites	10	10	20	20/20
Sponsored Internet sites	2	2	4	2/4
<i>"Pregnancy and morning sickness"</i>				
Non sponsored Internet sites	10	10	20	17/20
Sponsored Internet sites	2	2	4	2/4
<i>"Pregnancy and nausea"</i>				
Non sponsored Internet sites	10	10	20	16/20
Sponsored Internet sites	1	1	2	1/2
The overall amount of non sponsored Internet sites	51	50	101	60
The overall amount of sponsored Internet sites	10	14	24	6

Fifty-nine percent (60/101) of the non sponsored Web sites were unique Web sites, whilst only 25 % (6/24) of the sponsored Web sites had this feature. An interesting observation that partly explain this difference was made when the search term

“morning sickness” was entered into the Yahoo search engine. The search term resulted in 8 sponsored Web sites. Two of the site names appeared twice on the result page, and when all eight sponsored links were investigated it was revealed that three different site names essentially had identical layout and information. These three sites were therefore defined as one, unique Web site. So, of the eight sponsored results, five led to the same Web site. This was not encountered in any of the other searches.

Figure 4.1.1 shows a flow chart of the relevance investigation of the 66 sites.

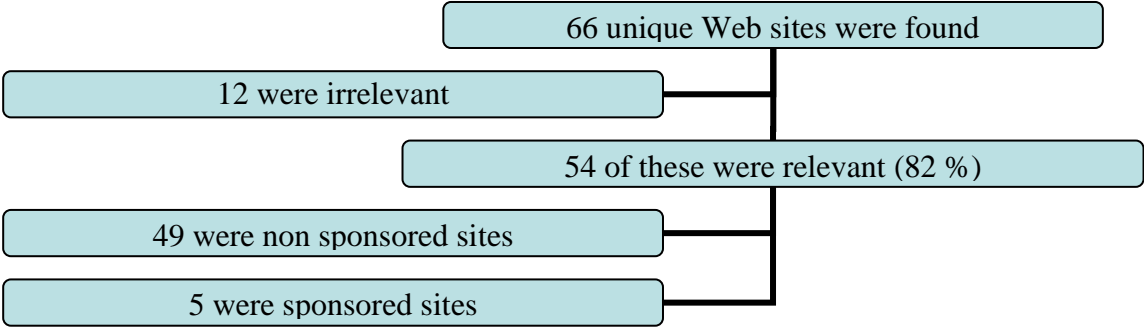


Figure 4.1.1 Flow chart of the relevance investigation of the 66 unique (duplicates removed) Web sites found

Figure 4.1.1 shows that 82 % of the Web sites were relevant, and so the search terms in figure 3.1.1 were appropriate when looking for NVP treatment suggestions.

The criteria for being in the “relevant” category were that the Web site contained information about NVP and suggested one or more treatments. Also, the information and treatments suggested had to be relatively easily accessed. Twelve of the sites were considered irrelevant. These were a list of books with morning sickness as the subject, a YouTube video of a pregnant game character throwing up and chat forum where anybody can post, thus making it impossible to retrieve all treatment suggestions. Sites with other topics than NVP were also found, and these were of course irrelevant.

All five relevant sponsored sites recommended acupressure in different forms, i.e. wristbands/"seasickness bands" or manual pressure onto certain points of the body. Only one mentioned that dietary changes were an option. All were retail sites.

Table 4.1.2 lists the treatment suggestions, precautions regarding these and some features of the non sponsored sites. The sponsored sites are not included in this table, since it is uncertain if people would trust the information provided by these transparent commercial sites (86).

Table 4.1.2 The relevant non sponsored Web sites and their treatment suggestion(s), precaution advices and selected site features

Treatment suggestion	Google		Yahoo		Unique Web sites	
	N=30	%	N=34	%	N=49	%
Dietary/practical advices	28	93,3	34	100,0	47	95,9
Acupressure	22	73,3	22	64,7	34	69,4
Ginger	21	70,0	17	50,0	30	61,2
Vit. B ₆	19	63,3	20	58,8	29	59,2
Medications	14	46,7	12	35,3	18	36,7
<i>See doctor before use of:</i>						
All supplements/medications	5	16,7	4	11,8	7	14,3
Ginger	3	10,0	4	11,8	5	10,2
Acupressure	1	3,3	1	2,9	1	2,0
Vit. B ₆	3	10,0	3	8,8	4	8,2
Medications	2	6,7	2	5,9	2	4,1
<i>Other features</i>						
Information about HG*	20	66,7	22	64,7	33	67,3
Retail	10	33,3	17	50,0	20	40,8
Last updated information	20	66,7	17	50,0	29	59,2
References	13	43,3	12	35,3	20	40,8
Author named	11	36,7	11	32,4	18	36,7
Health personell as author(s)	19	63,3	16	47,1	28	57,1

* Hyperemesis gravidarum

Changing the diet and other practical measurements was by far the most frequent recommendation, mentioned by 95.9% of the unique sites. Then followed: acupressure (69.4%), ginger (61.2%), vitamin B₆ (59.2%) and use of medications (36.7%).

Google results were prone to recommend ginger more often than Yahoo results, (70% : 50%)

In table 4.1.3 it can be seen that few of the sites that suggested ginger as a treatment option actually reported what amounts of ginger that could be consumed. Of the sites that did, daily dosage ranged from 250 mg three times daily and up to 1.5 gram daily, so all nine were reasonable when comparing with the amounts that have been used in the study of ginger as an anti-emetic (52;53;56-59).

Table 4.1.3 The sites that suggested ginger as a NVP treatment and the frequency of submitting a daily dose recommendation

	Google	Yahoo	Unique pages
	N=21	N=17	N=30
Providing a daily ginger dose recommendation	6	5	9

Because a rather large percentage of the non sponsored sites were retail, it was decided that a comparison between retail and non retail sites would be of interest. Also the five sponsored sites were included. The Yahoo and Google results have been aggregated due to a small individual sample size. The treatment suggestion results from this comparison can be seen in figure 4.1.2, and site feature comparison is shown in figure 4.1.3.

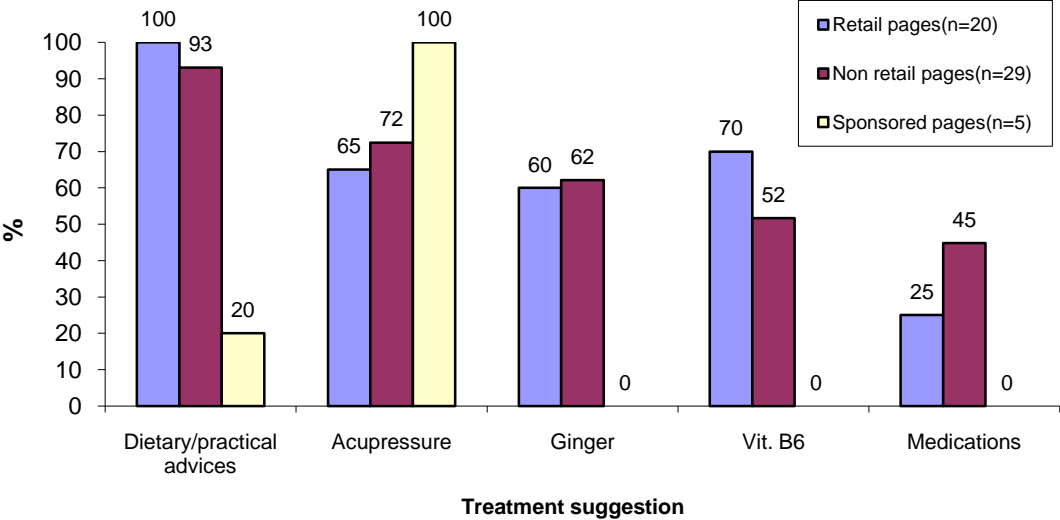


Figure 4.1.2 Comparison of what NVP treatments the retail, non retail and sponsored sites suggested

Figure 4.1.2 illustrates the main difference between the sponsored sites and non sponsored sites. All five sponsored sites tried to convince the Internet searcher to purchase either acupuncture wristbands or a book illustrating how acupuncture should be applied. No conclusion could be derived from the comparison of retail and non retail non sponsored Web sites. Retail sites recommended vitamin B₆ (14/20) more often than non retails did (15/29), whereas the non retails suggested medications (13/29) more often than the retail sites did (5/20). This tendency is further discussed in “5.2 Internet-suggested NVP treatments”.

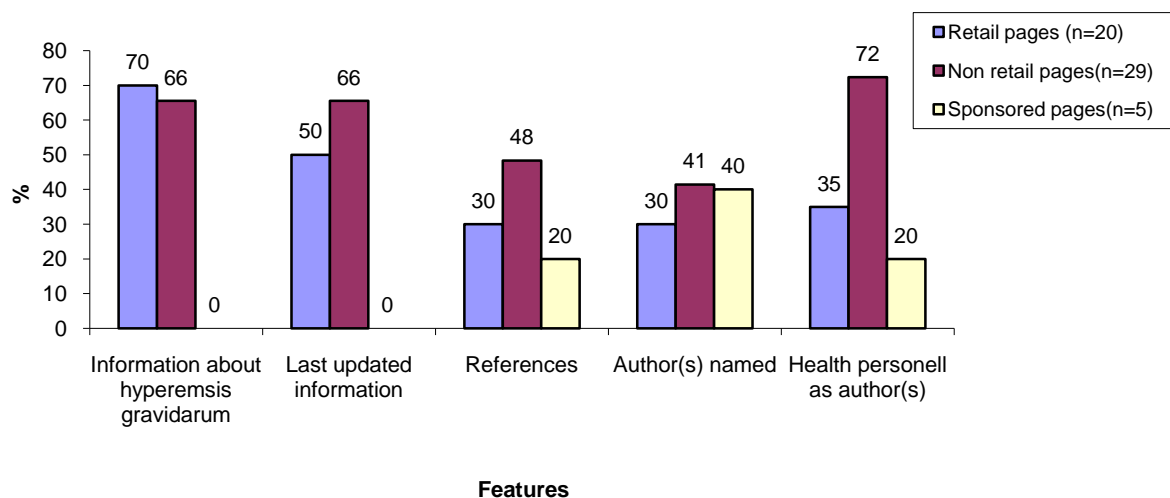


Figure 4.1.3 Selected site features for retail; non retail and sponsored sites were also compared

Figure 4.1.3 illustrates large differences between the three groups for some features. Sponsored sites did not inform about or state symptoms of hyperemesis gravidarum, or provide information on when the information last had been updated. They were also the group with lowest percentage reference information (n=1) and having health personnel as authors (n=1). Two of them named the author(s); this was the only feature where they were on the same percentage level as the two other groups. Non retail sites were the group that had most health personnel as author(s) (n=21), whilst only seven retail sites had this feature. Non retail sites also informed on the sources of information used more often than the two other groups (n=14). Six retail sites provided such information. Nineteen of the 29 non retail sites informed on when the site last had been created and/or modified, 10 of the retail sites also had this feature. If the selected features are perceived as signs of trustworthiness it seems that non

retail sites are most reliable, followed by the other two groups where retail was possible. (All five sponsored sites were retail.)

4.1.1 Statements from sponsored Web sites

Three quotes from sponsored Web sites that sold acupressure wristbands or a guide to how this could be performed using own hands are given. These quotes illustrate some of the arguments made in order to get the pregnant woman to purchase their product.

Spelling and grammar errors have not been corrected.

1: *“In a day and age when many medications receive bad publicity and get removed from the market after they are proven to be dangerous, a cure for morning sickness nausea that does not use any medications or chemicals is a welcomed weapon in the battle against morning sickness.”*

www.biobands.com/morningsickness/cures.htm

2: *“As a pregnant women, you likely prefer homeopathic solutions that you know will not harm you unborn child.”*

www.biobands.com/morningsickness/cure.htm

The sponsored Web site that appeared most frequently stated the following while describing the features of acupressure:

3: *“The technique is based on ancient chinese medicine. It might seem different from the treatment we normally get from our health care providers, but they really do not have much to offer when it comes to morning sickness.”*

www.cure-morning-sickness.com

The two first quotes are examples of the main marketing argument these sites had: use this natural and safe aid, avoid the dangerous medications. The second quote made little sense; is acupressure considered to be a homeopathic remedy? Nothing else was said on that topic. The third says that the health care system cannot provide helpful treatments, and this is used as an argument to try out a technique that scientists do not know how or if works.

4.1.2 The identical search procedure performed in Australia

As the links shown on the result page may differ based on the location of the searcher, the five search terms shown in figure 3.1.1 were also entered into Google and Yahoo by a person located in Australia. This was performed between February 3rd and February 8th, 2010.

www.google.com and *www.yahoo.com* was typed into the browser but was automatically altered to *www.google.com.au* and *http://au.yahoo.com*.

This is most likely the cause to why there were such a large proportion of site names with the national .com.au ending in these searches, whilst the .com ending was seen more in the original searches (performed in Norway).

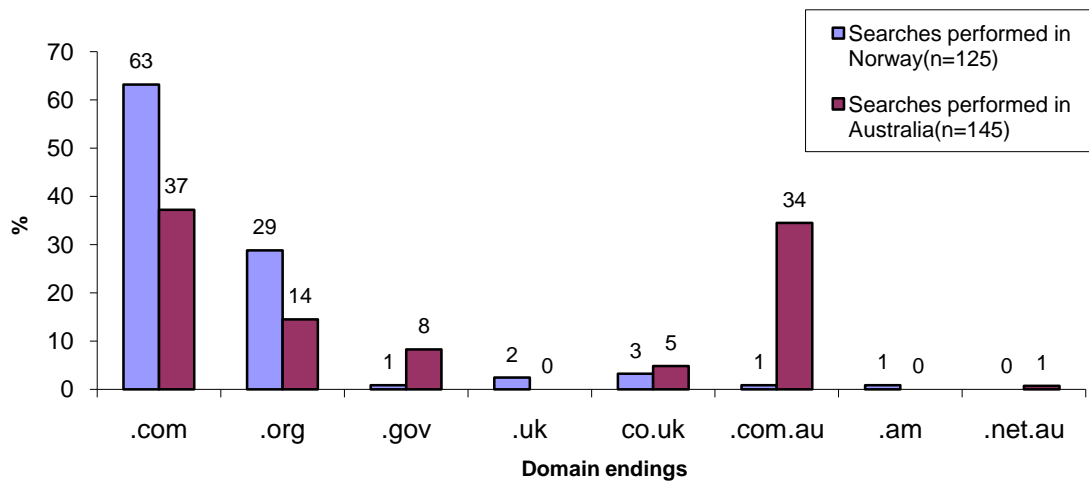


Figure 4.4 An illustration of the difference in domain endings when the search engine site ends with .com (Norwegian searches) and when it ends with .com.au or au.yahoo.com

It was not investigated if there were significant differences in content between the Australian and the Norwegian search results, as the main purpose of the Australian search was to illustrate that the searcher's whereabouts affects the Internet search results and thus may be a limitation to the transferability and generalisation of this study's information.

4.1.3 Statements about ginger

Few of the Web sites gave any advice on the safety of ginger use during pregnancy. One site that did not include ginger in its recommendations stated that more clinical studies had to be performed before anything about the safety and effect could be certain. None of the others gave any explanation for their exclusion. Of the Web sites that had ginger as a treatment

suggestion, four mentioned either that the use should be clarified with a doctor or used with caution. One said that the effect on the foetus was not investigated thoroughly.

Three selected Web site quotes are given below, because of their inter-individual differences.

“Herbal products such as Vitamin B₆ and ginger have also been used safely with varying degrees of effectiveness.”

www.motherisk.org/women/morningSickness.jsp

“There is some evidence to suggest that the supplement ginger may help to reduce the symptoms of nausea and vomiting in some pregnant women. And, to date, there have been no reports of any adverse effects caused by taking ginger during pregnancy.

However, in the UK, ginger products are unlicensed, so it is important that if you use ginger products, you ensure that you buy them from a reputable source, such as a pharmacy, or supermarket.”

www.nhs.uk

“Powdered ginger may help to relieve nausea and vomiting in some women. However, further studies are needed to confirm that this treatment is both safe and effective. Until more data are available, we suggest the use of ginger containing foods (eg. ginger lollipops, ginger ale) for mild nausea and vomiting.”

www.uptodate.com

www.motherisk.org is a program at The Hospital for Sick Children in Toronto. Motherisk counsel pregnant and lactating women, their family and clinicians on drugs, chemicals and environmental agents’ safety in these women (87).

www.nhs.uk: the NHS is the UK’s publicly funded National Health Service system.

www.uptodate.com is a clinical community that is updated three times a year; all information given is written and peer-reviewed by clinicians. The information comes from databases and journals (88;89).

Three statements, all from seemingly reliable sources, but regarding the use of ginger by pregnant women they provide different guidelines. The first also misclassify Vit.B₆ as a herb.

4.2 Results from the ginger retail sites

These searches were done to obtain information on what kind of sites that appears when looking for ginger retail, and if they contain any information on the safety and efficacy of ginger during pregnancy.

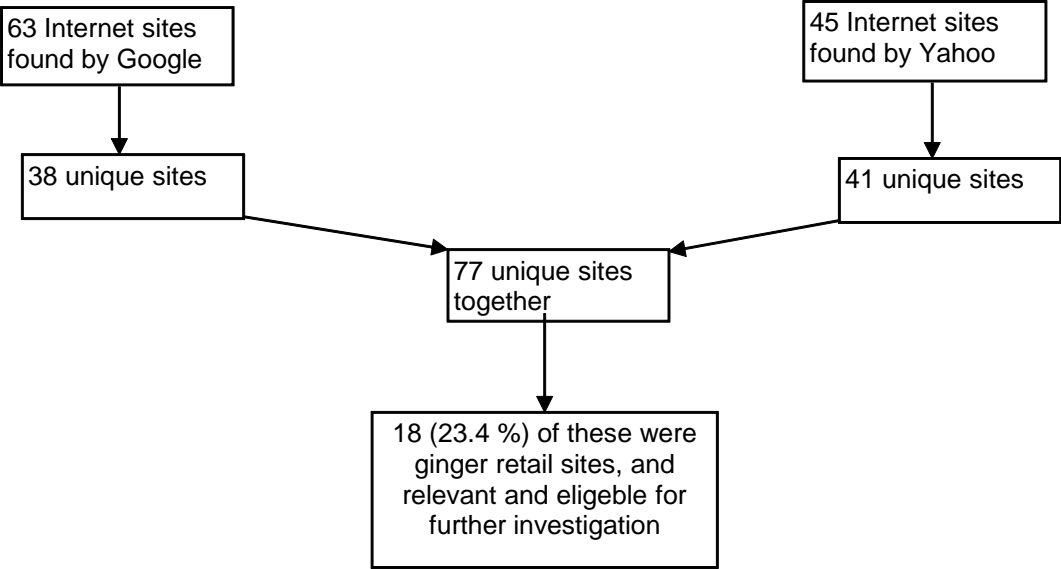


Figure 4.2.1 A flow chart illustrating the relevance assessment procedure of the search results

From figure 4.2.1 it can be derived that the search terms showed in figure 3.2.1 were not optimal for finding ginger retail sites. Only 23.4 % of the unique Web sites found were considered relevant.

The search terms may have been too unspecific, as many irrelevant retail sites appeared, selling anything from ginger kittens via software to wigs.

In figure 4.2.2 one can see that 58 % of the sites (n=11) were American, whilst 21 % (n=4) were either undeterminable or international companies.

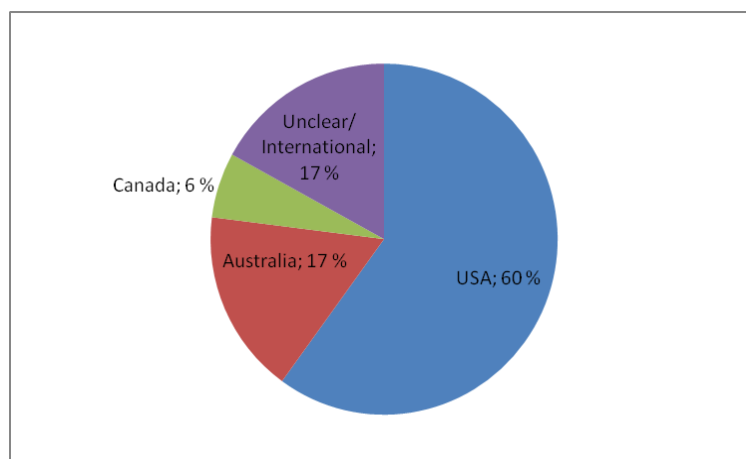


Figure 4.2.2 The nationalities of the 18 retail sites were investigated

Of the sites found, only the Australian sites had a national domain ending; the others were strictly .com sites and their nationality was identified in the “*about us*” section where this was available.

The retail sites and their statements about ginger and pregnancy are presented in table 4.2.1. If a site mentioned both nausea in general and pregnancy-induced nausea it was recorded in both categories.

Table 4.2.1 The opinions stated by the 18 sites regarding ginger use for nausea, and ginger use for nausea during pregnancy and also providing references for this information

Expressed opinions and use of references	N=18	%
"Ginger can be used against nausea"	10	55,6
"Ginger can be used against nausea by pregnant women"	5	27,8
No mention of neither nausea or pregnancy-induced nausea	7	38,8
References given	4	22,2

The sum is greater than 18 because some sites mentioned both nausea and pregnancy-induced nausea

It was looked specific for the words *nausea*, *morning sickness* and *nausea during/in pregnancy* when indications for use were investigated. The more general term often used, “*soothe an upset stomach*” and variants of this was frequently given on sites, but not categorized as “*ginger can be used against nausea*”.

Table 4.2.1 shows that *nausea* was given as an indication where ginger use was relevant by 10 sites (55.6 %). Five (27.8 %) mentioned *morning sickness* or similar. Few gave references for the provided information (n=4).

Only one site stated that the ginger product was not to be used during pregnancy and lactation, unless a healthcare practitioner had directed it. Another site said it was safe for short term use during pregnancy. The others neglected to give any such information.

4.3 The Internet searches performed in order to obtain information about the safety of ginger use during pregnancy, and its efficacy against NVP

Most of the Web sites from the safety/efficacy searches were relevant in the sense that they contained information about the safety of ginger use during pregnancy. Of the 22 Web sites, only two were excluded because of irrelevance. Due to a small sample size, the results from Yahoo and Google are aggregated.

Yahoo gave 10 site results on the first search result page, and all were found relevant. No sponsored results appeared. Google had 12 Web sites on the first search result page, of which two were sponsored and not relevant. One was an invitation to take part in an online survey, the other was an organisation for “high risk mothers” that may provide the information searched for, but the site shown contained no relevant information.

A total of 20 Web sites were relevant. Three of these appeared on both Google and Yahoo, so 17 unique Web sites were the result of these searches. One site only contained information about the effectiveness of ginger against NVP, and said nothing about the safety of use.

Figure 4.3.1 shows the proportion of sites that were “consumer” orientated and of a more scientific nature.

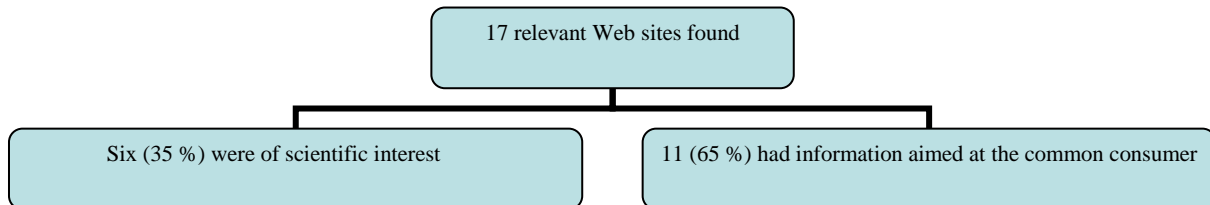


Figure 4.3.1 The nature of the sites found, illustrating that the searcher can choose between consumer-aimed information and more scientific based information

The nationalities of the sites were also recorded. The results are given in table 4.3.1, illustrating that the majority was American.

Table 4.3.1 The origin of each of the 17 Web sites that were found relevant

	USA	North-America	UK	Unknown
N=17	12	1	1	3

Figure 4.3.2 shows how many sites that stated that it was safe/uncertain/unsafe to consume ginger during pregnancy, and how many sites that stated that ginger is effective/uncertain effect/not effective against NVP. One consumer site said nothing about ginger’s efficacy against NVP, and so n = 10 for the “efficacy” consumer group

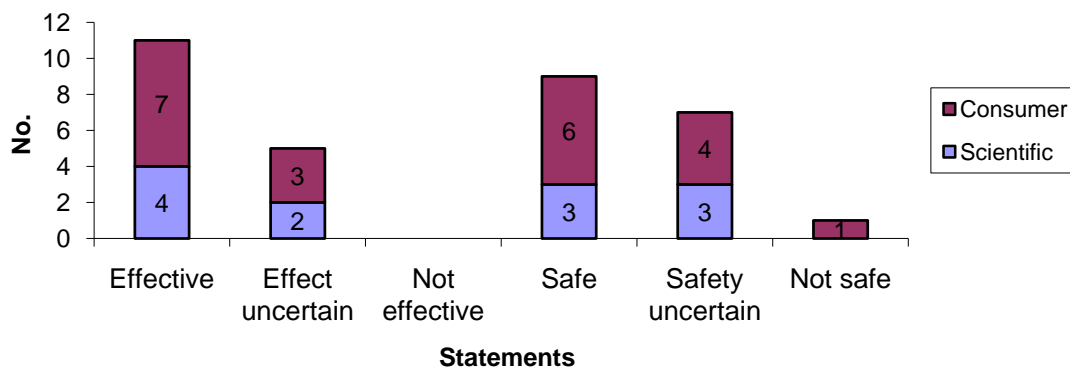


Figure 4.3.2 The majority of the 17 relevant Web sites stated that ginger use during pregnancy is an effective measure against NVP, and that it is safe to use

Figure 4.3.2 shows that 11/17 of the relevant Web sites found that ginger was an effective measure against NVP, and 9/11 also meant that it could be used safely by pregnant women. A large proportion (7/17, 41 %), stated that it was uncertain if ginger can be used safely by pregnant women (so the sample population is almost split at the middle).

None of the sites thought that ginger is not effective against NVP.

Figure 4.3.3 shows that 47 % (n=8) of the sites found ginger both safe for use during pregnancy and effective against NVP. The second largest group was the sites that were not convinced about neither effect nor safety (n=4, 24%), followed by the “*effective but safety uncertain*” –group (n=3, 18%).

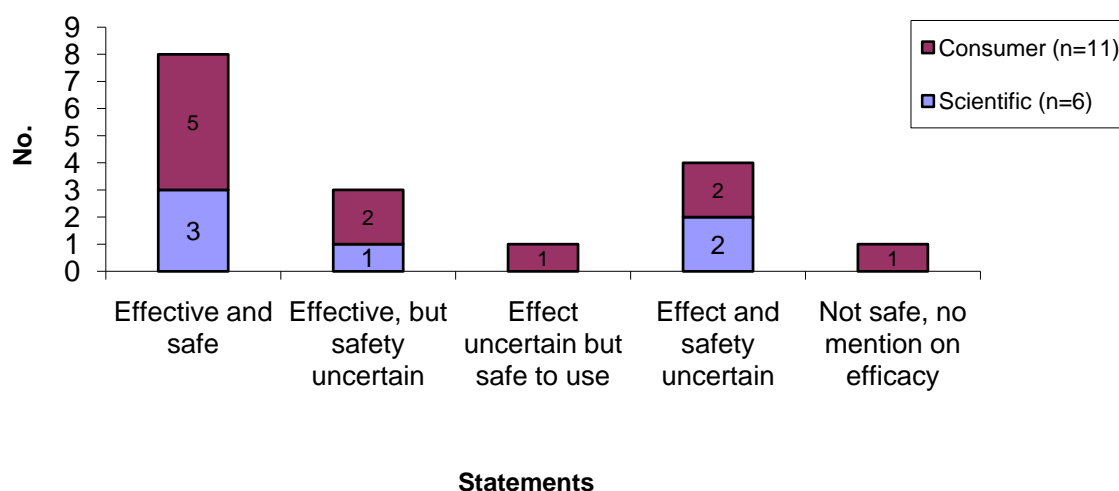


Figure 4.3.3 Ginger’s efficacy against NVP and its safety during pregnancy

Figure 4.3.3 shows the safety and efficacy opinions aggregated, and it can be seen that the six sites of a scientific nature were split at the middle regarding ginger's safety; three said it was safe and three said it was uncertain if it was safe for pregnant women to use. Four found ginger to be efficient against NVP, and all which found ginger safe also found it effective. Two consumer-sites found ginger to be effective, but did not find the data on the safety during pregnancy convincing. Taking ginger products during pregnancy was strongly advised against on one site. It is difficult to extract any differences between the scientific and the consumer-aimed sites from this dataset.

An interesting finding was also made; only one of the relevant unique sites was a retail site.

5. Discussion

5.1 Method

The method used in this study is inspired by other studies where the marketing of herbal products have been investigated, and where simulation of a consumer's Internet habits has been performed (32-34;37).

The increasing popularity and use of herbal products and the fact that the Internet is one of the most important and frequently used information sources for many people in the Western World was the base background of this study. It was mainly performed to find out if and how ginger is marketed on the Internet as a NVP treatment for pregnant women. Little, if any research on this field exists. A search in the database EMBASE in April, 2010 combining the words "*ginger*", "*internet*" and "*marketing*" did not result in any literature on this. An identical search in the MEDLINE database returned with three hits. None of these contained information on the topic addressed by this study. NVP is the most common pregnancy-related complaint (40), and it is estimated that 50-80 % of the women experiences this (41;42). Research on what kind of treatment these women are given by their doctor or choose themselves has been performed, and ginger has been found to be a popular aid (67-69). This study contributes to this area of research with knowledge on what the Internet provides of information on NVP treatments, and how ginger is portrayed regarding its efficacy against NVP and safety during pregnancy.

While planning the study, investigating ginger retail sites was perceived as the most interesting and important part. However, as the Internet searches and investigation of the results pages were performed, this opinion changed. Both the fact that the NVP treatment suggestion sites contained interesting features and that the searches done to obtain ginger retail sites resulted in few relevant sites played a part in this shift.

It was decided to use two search engines; Google and Yahoo. These two were selected on the basis of their popularity (5;6). The investigation of each Web site was performed several times, due to the fact that several features were found to be of interest as time passed. Naming the author(s) and stating their profession and for what treatments seeing a doctor before

initiating the treatment were recommended are examples of such features that initially was not included.

A positive side effect of only having two material sources was that these two could easily be compared regarding their features. In table 4.2 such a comparison between Google and Yahoo is shown. This was however not one of the aims of the study, as the material in some parts of the study was small. When there only are a few relevant Web sites (See figure 4.2.1 and 4.3.1), such a comparison is of little value.

The main reason for separating the results from sponsored and non sponsored sites was that little is known on sponsored Web sites; do people visit them or not? Most articles where the quality of Internet advices has been investigated do not state if sponsored sites has been included in their data or not. Also, even though few sponsored sites were found relevant it was interesting to see the tendency in this material versus the non sponsored sites, especially when it came to NVP treatment suggestions. All the sponsored sites recommended acupuncture, and only one included one other suggestion. Amongst the non sponsored there were much more diversity in the treatment suggestions.

For the ginger retail sites, this separation between sponsored and non sponsored sites was not found appropriate. The thought was that when a purchase is the goal, sponsored sites are more likely than in other situations to be visited as these are commercial.

The choice to investigate Web sites in English in general, not limiting it to sites from a specific country, made it difficult to investigate the legality of claims and statements. This was not done in this study.

The decision on which treatment suggestions to include in the material was made after the first investigation. The five that were included; practical/dietary changes, acupuncture, ginger, vitamin B₆ and medications, dominated other suggestions that were encountered.

Ginger was sometimes recommended in forms of cookies, ale, lollipops and similar products. Such recommendations were not included in the ginger-recommendation category. The ginger content in such products is questionable; a positive effect could be due to a raise in blood sugar level since nibbling on cookies will lead to this. The amount of ginger ingested is not

likely to be near the amounts that have been used in clinical trials, and so consuming these products is considered safe.

The identical searches performed in Australia were merely performed to see if there was a difference in what kind of Web sites that were shown, it was not for investigating different treatment suggestions although this could have been interesting.

5.2 Internet-suggested NVP treatments

It seems that the five search terms in table 4.1.1 were suitable for this investigation, as 54 of the 66 unique sites (82 %) were relevant.

All but two non sponsored sites suggested making some dietary and practical changes for relieving the NVP (table 4.1.2). This high recommendation rate of a non harmful aid is positive, showing pregnant women that altering the diet and meal frequency is an option that should be applied before other measurements are taken.

Duplicate sponsored Web sites were frequent; table 4.1.1 shows that of the total 24 found, only six were unique sites. This is not surprising; as such sites are related to phrases or key words. If either of these are entered into a search engine which the company has an advertising agreement with, their ad will appear. Apparently the five search terms used in this study matched with many of the same Web sites. The term “*morning sickness*” had the highest number of sponsored sites ($n = 8$). However, five of these led to the same Web site. Of the five, there were three different domain names. A possible explanation could be that the company figures that the consumers are attracted to different domain names and so the chance that the consumer will choose one of the company’s Web sites is increased.

The comparison of NVP treatment suggestions between sponsored sites and non sponsored sites, subdivided into retail and non retail sites showed a tendency to that sponsored sites suggested few different aids. All but one suggested only acupressure without even mentioning changes in diet and lifestyle. This narrow perspective can be said to be both positive and negative. It can be argued that these sites “*stick to what they know*”; acupressure. But not including even dietary and practical advices is perhaps too narrow a perspective.

Mentioning that this aid was completely safe and natural as often as possible seemed to be a tactic amongst these sites. Avoiding the use of medicines was stated as positive, and “*drug free*” was used as part of the slogan on one site. It can not be argued that unnecessary medical treatment of pregnant women (and everyone else) is to be avoided, but many pregnant women erroneously think that all medications are harmful for the foetus (67;70). The foetus is most often better off having a healthy mother and this fact needs to be appreciated and conveyed. Figure 4.1.3 show that none of the sponsored sites gave any information on hyperemesis gravidarum, which is a rare but important and serious condition (90). This complication of NVP is worth mentioning on all Web sites and other information sources and materials that deals with NVP. The fact that all of the five sponsored sites omitted such information while 33 out of the 49 non sponsored sites included it lowers sponsored Web sites credibility. However, it should be emphasised that five sponsored Web sites is a very small sample, and so to draw any conclusions from this is not recommended. The tendency is reported, and further investigation is needed to confirm or disprove this finding. When five different search terms entered into two different search engines only resulted in five unique sponsored sites, it can be difficult to obtain a much larger sample.

Sites that were non retail mentioned anti emetic medicines more often than retail sites. A speculation could be that since medications are not primarily to be sold via the Internet, it is not worth while mentioning such aids for sites that want the consumer to purchase products from them. Vitamin B₆ that can be sold on the Internet was more often suggested than on the non retail sites, but for the other suggestions there were minor differences.

The feature with the greatest difference was the “*health personnel written*” category. More than double of the non retail sites had this feature compared to the retail sites. Also in giving references and naming the author, non retail sites ranked higher. These features have been mentioned as “quality marks” in the DISCERN instrument (8), and so the non retail sites could be perceived as having a higher standard than the retail sites and sponsored sites.

5.2.1 The reliability of the sites

Both the searches performed in Norway and in Australia found most .com sites, which are commercial sites. The domain ending .org also appeared frequently (figure 4.4). Since anyone who wishes can register a .com or a .org domain there is nothing guaranteeing the quality of

the content. The Internet searcher must look for other features that can justify trusting the information given.

If a person investigates several different sites in order to double-check the treatment suggestions, he or she is likely to find similar advices on most of the sites and will probably trust the information given. Since ginger is recommended by many sites (n = 30, table 4.2.1) many will assume that it is totally safe to use, even though the safety information given is scarce. Nine of these 30 sites provided a daily dose recommendation, which is disappointingly low. When something that can be ingested is recommended it is, or at least should be natural, to add in what amounts this is appropriate.

In a quote shown in the Results section, vitamin B₆ was wrongfully included in the category “herbal products”. The source of this quote is perceived to be highly reliable by professionals, and even though this misclassification won’t affect the pregnant woman, it illuminates that errors exist even on “quality” sites.

Even though table 4.1.2 show that 20 of the 49 unique non sponsored sites had references for the provided information, the references given were often of little use. When it is not clarified what reference that contain which information, double-checking the site information with the reference information is difficult.

It would have been interesting to divide these site results into a scientific group and a consumer aiming group as in the safety information search to see if there are quality differences. This was however not thought of in time.

5.2.2 Ginger safety

Few sites mentioned anything about the safety of ginger. Of the 30 sites that recommended ginger, four said to use it cautiously or clarify it with a doctor. From the three quotes presented in the result section on page 30 it is seen that a seemingly reliable and professional site did not find the safety and efficacy data on ginger to be sufficient enough, and suggested

that ginger in food and beverage could be used, but powdered ginger should be avoided. Ginger lollipops and ginger ale were given as examples that were accepted. Both are rich in sugar, and it has been proposed that a rise in the blood sugar level can help alleviate NVP symptoms (55). It is therefore almost impossible to find out if an effect is due to ginger or the sugar, and also the amount of ginger consumed is difficult to determine.

The other two quotes are also a bit puzzling; first vitamin B₆ is misclassified as a herb, and next the supermarket is considered a reputable source for ginger products. At a supermarket, the ginger customer will likely receive no advice or precautions at all. On the plus side, the pharmacy is also considered reputable; and one can assume the ginger customer will get some kind of advice there. Not considering (at least not mentioning) health stores to be a reliable source of herbal products is interesting. One speculation could be that it is considered better to purchase herbal products and receive no advice than receiving potential ill advice at health food stores, as this has been found to happen (82;83).

5.3 Ginger retail sites

The chosen search terms turned out to be too unspecific, returning sites that sold any thinkable and unthinkable products containing the word “ginger”. Only 19 out of 77 unique Web sites were relevant (24.7 %). In hindsight, more specific terms should have been applied; perhaps “ginger capsules” and/or “herbal” could have been included. Experiencing this was however not a waste of time, but a simple way of illustrating that the Internet sometimes can be a jungle, where navigation is difficult.

Table 4.2.1 show that few of the 18 sites actually recommended ginger products for use against NVP (n = 5). The term “nausea” was a more frequent mentioned indication (n = 10). Different variations of “upset stomach” were seen on almost all of the sites, and the impression that was left after the investigation was that ginger is safe to use. This was mainly based on the fact that all but two neglected to say anything about whether or not it was safe for pregnant women, or said it could be used against morning sickness. Of the two that stated an opinion, they differed in the opinion. One said it was safe to use by pregnant women over a short period of time, whilst the other said it was only to be used with the consent of a health care practitioner.

Also, ginger seemed to be a marvellous aid for a variety of conditions. It could supposedly be used against cancer, as an aphrodisiac, to remove toxins from the body, treat asthma and so on according to one site. Other sites also listed up various properties.

The scarce amount of information on ginger's safety during pregnancy is disappointing. One could say that leaving such information out is the same as saying it is okay to use it. One can not expect retail sites to come up with a detailed overview of the research that exists on ginger and NVP is, but a note saying that pregnant women should talk to qualified health personnel before taking the product is reasonable to expect.

Table 4.2.1 also show that four out of the 18 sites provided references for the information that was given. A problem is however that these "references/sources" often is a list that does not specify which information that comes from the different sources. It is therefore difficult for the reader to investigate the sources if this is desired.

5.4 Information on the safety and efficacy of ginger

It can be seen in figure 4.3.1 that the study sample in this part of the study was small.

None of the sites found that ginger was inefficient against NVP, but five found that more research was needed until its effect could be verified.

Regarding ginger use by pregnant women and the safety of this, the study sample was almost split in halves. Of the 17 sites, seven said that it was uncertain if such use is safe or not, nine said "safe" and one conclusively said ginger was not safe for pregnant women.

It is an aim to clarify to the public that "natural" does not equal "safe". But it is difficult both for pregnant women and health personnel to make up his or her mind on ginger when the available information on its safety is so different in opinions. Since studies have found that many Internet searchers like to double-check the information on one site with another site (2), these people will end up very confused. Pharmacists, midwives and doctors needs to be up for the task to guide pregnant women to the appropriate aid(s).

It was interesting that only one of the 17 relevant unique sites was a retail site. When safety is specific searched for, the result site was no longer a mix of retail and non retail sites but largely dominated (94%) by non retail sites.

5.5 Limitations of the study

All sites were investigated by the same person; perhaps the findings could have been assessed by another researcher to see if there was coherence between the two. It is however not likely that this fact would have led to significant changes in the results, since the information and features investigated were specific. For example, a site either suggests ginger as a NVP treatment or it does not. There is no in-between.

Since it has been shown that the Internet searcher's whereabouts affect the results on the result site both previously and in this study, one could imagine that pregnant women in some areas will run into sites with consistent advice on the safety and efficacy of ginger.

6. Conclusion

Ginger is suggested frequently as a NVP treatment on the Internet. The majority of sites recommending ginger were commercial.

The information on ginger's safety during pregnancy was scarce, and amongst sites of a professional nature, the advices given on ginger's safety differed. This could be due to national guidelines and traditions.

When a specific search on the safety and efficacy was done, the majority of sites found ginger to be both effective against NVP and safe to use for pregnant women. This material was however of a small size. Only one retail site was found in this specific search.

Online purchase of ginger was offered by many sites, but when browsing for such retail sites one must be very specific in the search terms used in order to find the relevant sites, or directly go to retail sites one already knows about. Very little information on ginger is provided by the retail sites.

Since the pharmacy is an arena that is trusted and easily accessible to the public, pharmacists must know where to find the appropriate information on herbal products so that they are capable to counsel and give advices to customers and patients. A precaution about the lack of quality assurance of Web sites should be included.

7. References

Front page illustration of *Zingiber officinale* Roscoe:
<http://www.botanical.com/botanical/mgmh/g/ginger13-1.jpg>

Figure 1.6.1 : <http://liveliving.wordpress.com/2009/08/>

Reference List

- (1) Fox S, Pew Internet & American Life Project. Online Health Search 2006. <http://www.pewinternet.org/Reports/2006/Online-Health-Search-2006.aspx?r=1> 2006 [cited 2010 Mar 18];
- (2) Eysenbach G, Kohler C. How do consumers search for and appraise health information on the world wide web? Qualitative study using focus groups, usability tests, and in-depth interviews. *BMJ* 2002 Mar 9;324(7337):573-7.
- (3) Declercq ER, Sakala C, Corry MP, Applebaum S. Listening to Mothers II: Report of the Second National U.S. Survey of Women's Childbearing Experiences: Conducted January-February 2006 for Childbirth Connection by Harris Interactive(R) in partnership with Lamaze International. *J Perinat Educ* 2007;16(4):9-14.
- (4) Peterson G, Aslani P, Williams KA. How do consumers search for and appraise information on medicines on the Internet? A qualitative study using focus groups. *J Med Internet Res* 2003 Dec 19;5(4):e33.
- (5) SEW staff. Top Search Providers for August 2009, US. <http://searchenginewatch.com/3634991> 2009 [cited 2009 Oct 25];
- (6) Laycock J. Google is the Most Popular Search Engine in the World. <http://www.searchengineguide.com/jennifer-laycock/google-is-the-m.php> 2007 [cited 2009 Oct 15];
- (7) Hays R, Molyneux A. Different Internet service providers produce different search results. *Medical Education* 2008 Sep;42(9):945.
- (8) DISCERN.org. The DISCERN Instrument. http://www.discern.org.uk/discern_instrument.php 2010 [cited 2010 May 15];
- (9) Charnock D, Shepperd S. Learning to DISCERN online: applying an appraisal tool to health websites in a workshop setting. *Health Educ Res* 2004 Aug;19(4):440-6.
- (10) Larsson M. A descriptive study of the use of the Internet by women seeking pregnancy-related information. *Midwifery* 2009 Feb;25(1):14-20.
- (11) Lagan BM, Sinclair M, Kernohan WG. A web-based survey of midwives' perceptions of women using the Internet in pregnancy: a global phenomenon. *Midwifery* 2009 Aug 21.
- (12) World Health Organization. WHO, Traditional medicine. <http://www.who.int/mediacentre/factsheets/fs134/en/> 2010 [cited 2010 Mar 24];

- (13) Tindle HA, Davis RB, Phillips RS, Eisenberg DM. Trends in use of complementary and alternative medicine by us adults: 1997-2002. *Alternative Therapies in Health and Medicine* 2005 Jan;11(1):42-9.
- (14) Thomas KJ, Nicholl JP, Coleman P. Use and expenditure on complementary medicine in England: A population based survey. *Complementary Therapies in Medicine* 2001;9(1):2-11.
- (15) Zhang AL, Story DF, Lin V, Vitetta L, Xue CCL. A population survey on the use of 24 common medicinal herbs in Australia. *Pharmacoepidemiology and Drug Safety* 2008 Oct;17(10):1006-13.
- (16) Rafferty AP, McGee HB, Miller CE, Reyes M. Prevalence of complementary and alternative medicine use: state-specific estimates from the 2001 Behavioral Risk Factor Surveillance System. *Am J Public Health* 2002 Oct;92(10):1598-600.
- (17) Singh SR, Levine MA. Natural health product use in Canada: analysis of the National Population Health Survey. *Can J Clin Pharmacol* 2006;13(2):e240-e250.
- (18) Nowak D, Zlatic T. Herbal products and the Internet: a marriage of convenience. *J Am Pharm Assoc (Wash)* 1999 Mar;39(2):241-2.
- (19) Statens legemiddelverk (The Norwegian Medicines Agency). Kjøp på internett av medisiner, kosttilskudd og naturmidler (Online purchase of medications, dietary supplements and natural products). http://www.legemiddelverket.no/templates/InterPage____80212.aspx?filterBy=CopyToGeneral 2008 [cited 2010 Mar 14];
- (20) Bransjerådet for Naturmidler. Markedsdata (Market data). <http://brn.no/wsp/brn/webon.cgi?session=avfQBAXTxmHWvyjzS6LR8e0aSGUIA3&func=index> 2010 [cited 2009 Dec 2];
- (21) Statistics Canada. Canadian internet use survey, internet shopping, by type of product and service. <http://www40.statcan.gc.ca/101/cst01/comm24-eng.htm> 2008 [cited 2010 Mar 15];
- (22) Statistics Canada. Canadian Internet Use Survey. <http://www.statcan.gc.ca/cgi-bin/imdb/p2SV.pl?Function=getSurvey&SDDS=4432&lang=en&db=imdb&adm=8&dis=2#5> 2008 [cited 2010 Mar 15];
- (23) US Department of Commerce. A Nation Online: How Americans Are Expanding Their Use of the Internet. US Dept of Commerce 2002 [cited 2010 Mar 20]; Available from: URL: http://www.ntia.doc.gov/ntiahome/dn/nationonline_020502.htm
- (24) Muller D, Weinmann W, Hermanns-Clausen M. Chinese slimming capsules containing sibutramine sold over the Internet: a case series. *Dtsch Arztebl Int* 2009 Mar;106(13):218-22.
- (25) Statens legemiddelverk (The Norwegian Medicines Agency). Midlertidig tilbaketrekning av slankemidlet sibutramin - produktet trukket fra markedet

- (Suspension of marketing authorisation for sibutramine). http://www.legemiddelverket.no/templates/InterPage____81185.aspx 2010 [cited 2010 Mar 19];
- (26) Food and Drug Administration. FDA's MedWatch Safety Alerts: January 2010. <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm199585.htm#MeridiaRiskyforPeopleWithHeartDisease> 2010 [cited 2010 Mar 19];
 - (27) Ernst E. Adulteration of Chinese herbal medicines with synthetic drugs: a systematic review. *J Intern Med* 2002 Aug;252(2):107-13.
 - (28) Slifman NR, Obermeyer WR, Aloji BK, Musser SM, Correll WA, Jr., Cichowicz SM, et al. Contamination of botanical dietary supplements by *Digitalis lanata*. *N Engl J Med* 1998 Sep 17;339(12):806-11.
 - (29) Ries CA, Sahud MA. Agranulocytosis caused by Chinese herbal medicines. Dangers of medications containing aminopyrine and phenylbutazone. *JAMA* 1975 Jan 27;231(4):352-5.
 - (30) Ramsay HM, Goddard W, Gill S, Moss C. Herbal creams used for atopic eczema in Birmingham, UK illegally contain potent corticosteroids. *Arch Dis Child* 2003 Dec;88(12):1056-7.
 - (31) Lau KK, Lai CK, Chan AW. Phenytoin poisoning after using Chinese proprietary medicines. *Hum Exp Toxicol* 2000 Jul;19(7):385-6.
 - (32) Morris CA, Avorn J. Internet marketing of herbal products. *JAMA* 2003 Sep 17;290(11):1505-9.
 - (33) Tønnesen.M.H., Holst L, Haavik S. Markedsføring av naturmidler: Vurdering av annonser for dvergpalme- og tranebærprodukter (Marketing of natural health products: Investigation of advertisements for saw palmetto- and cranberryproducts). *Norsk Farmaceutisk Tidsskrift* 2010;(1):30-3.
 - (34) Whelan AM, Jurgens TM, Bowles SK, Doyle H. Efficacy of natural health products in treating osteoporosis: what is the quality of internet patient advice? *Ann Pharmacother* 2009 May;43(5):899-907.
 - (35) Bonakdar RA. Herbal cancer cures on the Web: noncompliance with The Dietary Supplement Health and Education Act. *Fam Med* 2002 Jul;34(7):522-7.
 - (36) FDA Issues Regulation Prohibiting Sale of Dietary Supplements Containing Ephedrine Alkaloids and Reiterates Its Advice That Consumers Stop Using These Products. Food and Drug Administration 2009 [cited 2010 Mar 18]; Available from: URL: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108242.htm>
 - (37) Ashar BH, Miller RG, Getz KJ, Pichard CP. A critical evaluation of Internet marketing of products that contain ephedra. *Mayo Clin Proc* 2003 Aug;78(8):944-6.

- (38) Shekelle PG, Hardy ML, Morton SC, Maglione M, Mojica WA, Suttorp MJ, et al. Efficacy and safety of ephedra and ephedrine for weight loss and athletic performance: a meta-analysis. *JAMA* 2003 Mar 26;289(12):1537-45.
- (39) Haller CA, Benowitz NL. Adverse cardiovascular and central nervous system events associated with dietary supplements containing ephedra alkaloids. *N Engl J Med* 2000 Dec 21;343(25):1833-8.
- (40) Sosial- og helsedirektoratet (Ministry of Health and Care Services. Kap.10 Alminnelige plager i svangerskapet (Chapter 10; Common pregnancy-induced problems). Retningslinjer for svangerskapsomsorgen. 2005.
- (41) O'Brien B, Zhou Q. Variables related to nausea and vomiting during pregnancy. *Birth* 1995 Jun;22(2):93-100.
- (42) Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting during pregnancy. *Br J Gen Pract* 1993 Jun;43(371):245-8.
- (43) Mason E, Routledge PA. Nausea and vomiting. In: Walker R, Whittlesea C, editors. *Clinical pharmacy and therapeutics*. 2007. p. 487-95.
- (44) American College of Obstetricians and Gynecologists. ACOG Education Pamphlet AP126 "Morning Sickness". http://www.acog.org/publications/patient_education/bp126.cfm 2010 [cited 2010 May 12];
- (45) Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev* 2003;(4):CD000145.
- (46) Ginger Monograph. *Natural Medicines Comprehensive Database* 2010 [cited 2010 Mar 19]; Available from: URL: <http://www.naturaldatabase.com/%28S%283uxglmzais510mbpiuw0linp%29%29/nd/SeArch.aspx?cs=&s=ND&pt=100&id=961&ds=&name=GINGER&searchid=19752557>
- (47) Barnes J, Anderson LA, Phillipson JD. *Ginger. Herbal Medicines*. Pharmaceutical Press; 1996.
- (48) Govindarajan VS. Ginger--chemistry, technology, and quality evaluation: part 1. *Crit Rev Food Sci Nutr* 1982;17(1):1-96.
- (49) Jolad SD, Lantz RC, Solyom AM, Chen GJ, Bates RB, Timmermann BN. Fresh organically grown ginger (*Zingiber officinale*): composition and effects on LPS-induced PGE2 production. *Phytochemistry* 2004 Jul;65(13):1937-54.
- (50) Jolad SD, Lantz RC, Chen GJ, Bates RB, Timmermann BN. Commercially processed dry ginger (*Zingiber officinale*): composition and effects on LPS-stimulated PGE2 production. *Phytochemistry* 2005 Jul;66(13):1614-35.
- (51) Jiang X, Williams KM, Liauw WS, Ammit AJ, Roufogalis BD, Duke CC, et al. Effect of ginkgo and ginger on the pharmacokinetics and pharmacodynamics of warfarin in healthy subjects. *Br J Clin Pharmacol* 2005 Apr;59(4):425-32.

- (52) Keating A, Chez RA. Ginger syrup as an antiemetic in early pregnancy. *Altern Ther Health Med* 2002 Sep;8(5):89-91.
- (53) Ensiyeh J, Sakineh M-A. Comparing ginger and vitamin B6 for the treatment of nausea and vomiting in pregnancy: a randomised controlled trial. *Midwifery* 2009 Dec;25(6):649-53.
- (54) Portnoi G, Chng LA, Karimi-Tabesh L, Koren G, Tan MP, Einarson A. Prospective comparative study of the safety and effectiveness of ginger for the treatment of nausea and vomiting in pregnancy. *Am J Obstet Gynecol* 2003 Nov;189(5):1374-7.
- (55) Tiran DMS. *Complementary Therapies for Pregnancy and Childbirth*. Second ed. Harcourt Publishers Limited; 2000.
- (56) Fischer-Rasmussen W, Kjaer SK, Dahl C, Asping U. Ginger treatment of hyperemesis gravidarum. *Eur J Obstet Gynecol Reprod Biol* 1991 Jan 4;38(1):19-24.
- (57) Vutyavanich T, Kraissarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. *Obstet Gynecol* 2001 Apr;97(4):577-82.
- (58) Sripramote M, Lekhyananda N. A randomized comparison of ginger and vitamin B6 in the treatment of nausea and vomiting of pregnancy. *J Med Assoc Thai* 2003 Sep;86(9):846-53.
- (59) Smith C, Crowther C, Willson K, Hotham N, McMillian V. A randomized controlled trial of ginger to treat nausea and vomiting in pregnancy. *Obstet Gynecol* 2004 Apr;103(4):639-45.
- (60) Verma SK, Singh J, Khamesra R, Bordia A. Effect of ginger on platelet aggregation in man. *Indian J Med Res* 1993 Oct;98:240-2.
- (61) Bordia A, Verma SK, Srivastava KC. Effect of ginger (*Zingiber officinale* Rosc.) and fenugreek (*Trigonella foenumgraecum* L.) on blood lipids, blood sugar and platelet aggregation in patients with coronary artery disease. *Prostaglandins Leukot Essent Fatty Acids* 1997 May;56(5):379-84.
- (62) Weidner MS, Sigwart K. The safety of a ginger extract in the rat. *J Ethnopharmacol* 2000 Dec;73(3):513-20.
- (63) Wilkinson JM. Effect of ginger tea on the fetal development of Sprague-Dawley rats. *Reprod Toxicol* 2000 Nov;14(6):507-12.
- (64) Weidner MS, Sigwart K. Investigation of the teratogenic potential of a zingiber officinale extract in the rat. *Reprod Toxicol* 2001 Jan;15(1):75-80.
- (65) Backon J. Ginger in preventing nausea and vomiting of pregnancy; a caveat due to its thromboxane synthetase activity and effect on testosterone binding. *Eur J Obstet Gynecol Reprod Biol* 1991 Nov 26;42(2):163-4.
- (66) Murphy PA. Alternative therapies for nausea and vomiting of pregnancy. *Obstetrics and Gynecology* 1998 Jan;91(1):149-55.

- (67) Hollyer T, Boon H, Georgousis A, Smith M, Einarson A. The use of CAM by women suffering from nausea and vomiting during pregnancy. *BMC Complement Altern Med* 2002 May 17;2:5.
- (68) Westfall RE. Use of anti-emetic herbs in pregnancy: women's choices, and the question of safety and efficacy. *Complement Ther Nurs Midwifery* 2004 Feb;10(1):30-6.
- (69) Baggley A, Navioz Y, Maltepe C, Koren G, Einarson A. Determinants of women's decision making on whether to treat nausea and vomiting of pregnancy pharmacologically. *Journal of Midwifery and Women's Health* 2004 Jul;49(4):350-4.
- (70) Mazzotta PM, Magee LAM, Koren GM. The perception of teratogenic risk by women with nausea and vomiting of pregnancy. [Miscellaneous]. *Clinical Pharmacology & Therapeutics* 1999 Feb;65(2):200.
- (71) Nordeng H, Havnen GC. Use of herbal drugs in pregnancy: a survey among 400 Norwegian women. *Pharmacoepidemiology and Drug Safety* 2004 Jun;13(6):371-80.
- (72) Holst L, Nordeng H, Haavik S. Use of herbal drugs during early pregnancy in relation to maternal characteristics and pregnancy outcome. *Pharmacoepidemiol Drug Saf* 2008 Feb;17(2):151-9.
- (73) Holst L, Wright D, Haavik S, Nordeng H. The use and the user of herbal remedies during pregnancy. *J Altern Complement Med* 2009 Jul;15(7):787-92.
- (74) Maats FH, Crowther CA. Patterns of vitamin, mineral and herbal supplement use prior to and during pregnancy. *Aust N Z J Obstet Gynaecol* 2002 Nov;42(5):494-6.
- (75) Pinn G, Pallett L. Herbal medicine in pregnancy. *Complement Ther Nurs Midwifery* 2002 May;8(2):77-80.
- (76) Forster DA, Denning A, Wills G, Bolger M, McCarthy E. Herbal medicine use during pregnancy in a group of Australian women. *BMC Pregnancy Childbirth* 2006;6:21.
- (77) Tsui B, Dennehy CE, Tsourounis C. A survey of dietary supplement use during pregnancy at an academic medical center. *Am J Obstet Gynecol* 2001 Aug;185(2):433-7.
- (78) Glover DD, Amonkar M, Rybeck BF, Tracy TS. Prescription, over-the-counter, and herbal medicine use in a rural, obstetric population. *Am J Obstet Gynecol* 2003 Apr;188(4):1039-45.
- (79) Moussally K, Oraichi D, Berard A. Herbal products use during pregnancy: prevalence and predictors. *Pharmacoepidemiol Drug Saf* 2009 Jun;18(6):454-61.
- (80) Ernst E. Advice offered by practitioners of complementary/ alternative medicine: an important ethical issue. *Eval Health Prof* 2009 Dec;32(4):335-42.
- (81) Ernst E, Schmidt K. Health risks over the Internet: advice offered by "medical herbalists" to a pregnant woman. *Wien Med Wochenschr* 2002;152(7-8):190-2.

- (82) Buckner KD, Chavez ML, Raney EC, Stoehr JD. Health food store's recommendations for nausea and migraines during pregnancy. *Annals of Pharmacotherapy* 2005 Feb;39(2):274-9.
- (83) Mills E, Ernst E, Singh R, Ross C, Wilson K. Health food store recommendations: implications for breast cancer patients. *Breast Cancer Res* 2003;5(6):R170-R174.
- (84) Koren G, Oren D, Rouleau M, Carmeli D, Matsui D. Comparison of verbal claims for natural health products made by health food stores staff versus pharmacists in Ontario, Canada. *Canadian Journal of Clinical Pharmacology* 2006;13(2):e251-e256.
- (85) TNS Gallup. ApotekBarometeret. <http://webcache.googleusercontent.com/search?q=cache:R1bIJJ-pYyAJ:hugin+info/135876/R/1003514/154188+ppt+apotekbarometer&cd=1&hl=no&ct=clnk&gl=no&client=firefox-a> 2009 [cited 2010 May 15];
- (86) Morahan-Martin JM. How internet users find, evaluate, and use online health information: a cross-cultural review. *Cyberpsychol Behav* 2004 Oct;7(5):497-510.
- (87) The Motherisk Team. The Motherisk Program. <http://www.obgyn.net/women/women.asp?page=/women/articles/motherisk> 1997 [cited 2010 May 15];
- (88) Medisinsk bibliotek UUMIUU. Kliniske oppslagsverk (Clinical reference work). www.ullevaal.no/stream_file.asp?iEntityId=26864 2010 [cited 2010 May 15];
- (89) UpToDate Inc. About UpToDate. <http://www.uptodate.com/home/about/index.html> 2010 [cited 2010 May 15];
- (90) Vorvick L, Storck S. Hyperemesis gravidarum. <http://www.nlm.nih.gov/medlineplus/ency/article/001499.htm> 2010 [cited 2010 May 1];