A QUICK LOOK AT HERCEPTIN FOR BREAST CANCER

Before we start

Bandolier has tended to avoid cancer studies in looking at evidence because it is a different world compared with most clinical situations. Cancer trials may be randomised, but they never compare a new treatment with no treatment; typically they compare the usual best care with usual best care plus the new treatment. Progress is measured in increments rather than great leaps forward.

Then there are the outcomes, of which there are many. Not dying comes to mind first of all. But there is also keeping the cancer at bay. Put these together and you have a new outcome, that of disease-free survival. And there are more like that, some of real importance to patients, others of great importance to oncologists.

Not unimportant is the duration of trials. This is cancer, after all, and we want to know what happens not after months, but years. So we often learn first about results after one year, then two, then five, and perhaps 10 at some later stage. That is good, because it maximises knowledge as soon as it is available, but initially we can only extrapolate about whether benefit at one year is maintained over later years, or increases, or evaporates.

And finally there is the issue of combinability. Cancer of even one organ is usually of many different types, and is treated differently at different stages of the disease. If we are lucky, we have a trial. We almost never have the luxury of meta-analysis.

And yet oncologists continue to improve cancer treatments, achieving not just longer survival or disease-free survival, but better quality of life. Bandolier is reminded of the friend with serious liver secondaries who boasted of living for four years with six months to live.

The point is that judging cancer trials and evidence isn’t easy. It requires time, hard work, and not a little insight. Bandolier has seen involved professionals ecstatic over trial results that leave purchasers of care wondering what the fuss is about.

In the full and certain knowledge that whatever we write, someone will take exception to some part of it, here is a quick look at trastuzumab (herceptin) for breast cancer, as readers have asked. Only published randomised trials in breast cancer are examined.

In this issue

<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herceptin and breast cancer</td>
<td>p. 1</td>
</tr>
<tr>
<td>DVT after knee arthroscopy</td>
<td>p. 4</td>
</tr>
<tr>
<td>Patent foramen ovale and migraine</td>
<td>p. 5</td>
</tr>
<tr>
<td>Barrett’s oesophagus incidence</td>
<td>p. 7</td>
</tr>
<tr>
<td>Grapefruit seed extract and health</td>
<td>p. 8</td>
</tr>
</tbody>
</table>

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Background

Trastuzumab is a monoclonal antibody to the extracellular domain of one of several receptor tyrosine kinases known as HER-2 that mediate growth, differentiation, and survival of cells. Over expression or amplification of the gene occurs in about 1 in 5 breast cancers, and is associated with aggressive progression. The idea is that blocking it should be a useful treatment for this form of breast cancer.

Trials of trastuzumab in FER-2 positive breast cancer have been reported both soon after initial diagnosis and treatment, and when the cancer has metastasised. These two circumstances will be examined separately. An important adverse event has been the development of congestive heart failure, which can be categorised as changes in cardiac function, symptomatic heart failure, or severe heart failure.

Early breast cancer

Three trials have been reported recently in two publications (Table 1), using treatment with different dose regimens of trastuzumab over one year, and with events reported at a median of one and two years. Although all the information for some trial arms has yet to be published, we have results on 5,060 women given trastuzumab as part of their treatment, and 2,372 women not given it.

The primary outcome was disease free survival, defined as absence of recurrence, a second primary event, or death without recurrence. Combining the information, one of these events occurred in 14% of women not given trastuzumab, compared with 8% of those who did receive it for a year. The relative risk was about 0.55 (95% confidence interval 0.5 to 0.6), and the number needed to treat 15 (13 to 19).

This combining of one and two year outcomes probably understates the benefit, though. In women who were observed for longer periods (up to three or four years), the benefits appeared to increase over time, with less disease recurrence or death compared with control. Based on very limited data and events, equivalent three and four year NNTs could be around 10 and 5. The benefits seemed to be similar in all subgroups or stratifications of women.

Set against the benefits was an increased rate of congestive heart failure. Symptomatic disease occurred in 2.4% of women on trastuzumab and 0.1% of controls, a relative risk of 16, and number needed to harm of about 45 (36 to 59). Only a small proportion of this was severe, though there were some cardiac deaths.

One other small trial used chemotherapy plus trastuzumab for six months before surgery for breast cancer, and found a complete clinical response in 21/23 women given the combination.

Metastatic breast cancer

For metastatic breast cancer there were four trials, one of which compared two regimens of trastuzumab in a kinetic plus clinical study. Typically, the trials involved women who had been treated initially with surgery, adjuvant chemotherapy, radiotherapy and hormones, but who had then developed a secondary metastasis about two years later. The trials compared one form of treatment (usually chemotherapy) with the same treatment plus trastuzumab, with treatment continuing until the disease progressed.

Complete response (disappearance of the secondary) occurred rarely, in fewer than 10% of women. Complete or partial response (shrinkage of tumour by a large amount) occurred in about 35%. Most women had stable disease, where the tumour neither grew nor shrank. Overall, the addition of trastuzumab increased the time to disease progression by three or four months, and overall survival by three to six months.

Adverse events

There were many adverse events associated with use of trastuzumab, both in early and metastatic breast cancer. Table 1 largely concentrates adverse event attention on symptomatic congestive heart failure, occurring in 2-3%.

Comment

The pattern of reporting for trastuzumab is not untypical of any new cancer treatment. Because cancer treatments are often toxic, they tend to be tried first in advanced breast cancer, then less advanced metastatic disease, and then only later as first line treatments in early breast cancer. That was the pattern with aromatase inhibitors, for instance.

In trials in cancer, time is the key. What we want to know about, namely improvements in survival, and especially disease free survival, can only be fully measured when patients have been followed up for many years. A trial with a five year follow up might take 10 years between design and reporting, not least because recruiting sufficient numbers itself takes time. And the better we get, the longer it takes to show big improvements.

So if there is nothing different between the trastuzumab reporting and what we have seen before, what about the results? In terms of the size of the benefits, they look quite good. Demonstrating an additional three months before progression in women with metastatic cancer is good. The results in early breast cancer, with a 50% reduction in bad events over one or two years are also rather good.

Lest anyone wonders at the disparity between these results, looked at with a cold and fishy eye or headlines in newspapers, it all depends on your point of view. In oncology terms these are very good results, and if the medicine were cheap everyone would be cheering. Because it is expensive, it presents real problems.

A word on costs

In metastatic breast cancer, a cost effectiveness analysis [1] estimates the total cost of treatment to be about €44,000 (£29,000). The cost per life year saved is between €63,000 and €162,000 (£42,000 and £108,000), calculated from survival improvements from trials. Reducing these figures...
Table 1: Summary of published randomised trials of trastuzumab (herceptin) in early breast cancer and metastatic breast cancer

<table>
<thead>
<tr>
<th>Reference</th>
<th>Women, previous treatment</th>
<th>Randomised treatment regimen</th>
<th>Beneficial outcomes</th>
<th>Harmful outcomes</th>
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<tbody>
<tr>
<td><strong>Early breast cancer</strong></td>
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<tr>
<td>Piccart-Gebhart et al. NEJM 2005 353: 1659-1672</td>
<td>5,081 women, 80% &lt;60 years (median 49 years), 16% premenopausal</td>
<td>Observation (n=1693) Trastuzumab 6 mg/kg every 3 weeks for 1 year (n=1694) Trastuzumab 6 mg/kg every 3 weeks for 2 years (n=1694) Median time between diagnosis and therapy initiation was 8 months</td>
<td>After average follow up 1 year Recurrence, second primary event Death without recurrence Observation: 13% Trastuzumab 1 year: 7.5% Trastuzumab 2 years at 1 year: 7.6%</td>
<td>Death any cause Observation: 2.2% Trastuzumab 1 year: 1.7% Severe CHF Observation: 0.0% Trastuzumab 1 year: 0.5% Symptomatic CHF Observation: 0.1% Trastuzumab 1 year: 1.6%</td>
</tr>
<tr>
<td>Romond et al. NEJM 2005 353: 1673-1684 (combined results All HER-2 positive)</td>
<td>3,351 women, 80% &lt;60 years Surgery plus chemotherapy, no metastases of two studies with 2 year median follow up)</td>
<td>Chemotherapy (n=1679) Trastuzumab 2 mg/kg weekly for 51 weeks (n=1672)</td>
<td>After average follow up 2 years Recurrence, second primary event Death without recurrence Chemotherapy: 16% Trastuzumab: 8.0% At 3 years disease free survival was 75% and 87% respectively, and at 4 years 67% and 85%</td>
<td>Death any cause Chemotherapy: 5.5% Trastuzumab: 3.7% Symptomatic CHF Chemotherapy: 0.4% Trastuzumab: 3.5%</td>
</tr>
<tr>
<td>Buzdar et al. J Clin Oncol 2005 23: 3676-3685</td>
<td>42 women, median age 50 years Chemotherapy before surgery All HER-2 positive</td>
<td>Chemotherapy alone (n=19) Chemotherapy + trastuzumab 2 mg/kg weekly for 24 weeks (n=23)</td>
<td>Clinical complete response: Chemotherapy alone 9/19 Chemotherapy + trastuzumab 21/23</td>
<td>No cases of CHF</td>
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<tr>
<td><strong>Metastatic breast cancer</strong></td>
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<tr>
<td>Marty et al. J Clin Oncol 2005 23: 4265-4274</td>
<td>186 women, median age 54 years, with median 4 metastases at median 2 sites, median of 25 months since diagnosis. Most with prior adjuvant chemotherapy, radiotherapy, hormonal therapy, All HER-2 positive</td>
<td>Docetaxel alone (n=94) Docetaxel plus trastuzumab 2 mg/kg weekly until disease progression (n=92) Docetaxel 6 cycles of docetaxel</td>
<td>Complete response: Docetaxel 2/94 Docetaxel + trastuzumab 7/92 Partial response: Docetaxel 32/94 Docetaxel + trastuzumab 54/92 Trastuzumab had significantly longer duration of response and time to progression (12 vs 6 months), and overall survival (31 vs 23 months)</td>
<td>Discontinuations because of adverse events: Docetaxel 20/94 Docetaxel + trastuzumab 9/92 Symptomatic CHF: Docetaxel 0/94 Docetaxel + trastuzumab 2/92</td>
</tr>
<tr>
<td>Baselga et al. J Clin Oncol 2005 23: 2162-2171</td>
<td>105 women with previously untreated metastatic breast cancer, median age 54 years, median disease duration 20 months, median metastatic sites 2. Most had adjuvant chemotherapy, hormonal, or radiotherapy. All HER-2 positive</td>
<td>Single arm trial, with trastuzumab 6 mg/kg every 3 weeks until disease progression, toxicity, or patient discontinuation</td>
<td>There were 2 complete and 18 partial responders. Median time to progression was 3.5 months</td>
<td>Symptomatic CHF in 1 woman</td>
</tr>
<tr>
<td>Vogel et al. J Clin Oncol 2002 20: 719-726</td>
<td>114 women, mean age 54 years, 1-4 metastatic sites. Most with prior adjuvant chemotherapy, radiotherapy, hormonal therapy. All HER-2 positive</td>
<td>Trastuzumab 2 mg/kg weekly (n=59) Trastuzumab 4 mg/kg weekly (n=55) Treatment continued until disease progression</td>
<td>An objective response was found in 26% of women, irrespective of dose Median time to disease progression was 3.5 months, and median survival 24 months</td>
<td>Cardiac dysfunction in 3 women</td>
</tr>
<tr>
<td>Slamon et al. NEJM 2001 344: 783-792.</td>
<td>234 women, mean age 54 years, with at least one metastatic site. Most with prior adjuvant chemotherapy, radiotherapy, hormonal therapy. All HER-2 positive</td>
<td>Chemotherapy 1 (n=138) Chemotherapy 1 + trastuzumab 2 mg/kg (n=143) Chemotherapy 2 (n=96) Chemotherapy 2 + trastuzumab (n=92) Treatment continued until disease progression</td>
<td>Addition of trastuzumab to chemotherapy increased median survival by almost 3 months, and gave lower death rate at 1 year (22% vs 39%)</td>
<td>Heart failure occurred in 22/234 women given trastuzumab, compared with 5/230 with chemotherapy alone</td>
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</tbody>
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would require large reductions in the cost of the drug, or larger improvements in survival. Costs of adverse events were not included. Costs in early breast cancer would be only a guess, and cost effectiveness is bound to be much less than TNF-alpha antibodies in early rheumatoid arthritis, for instance.

Of course, only 1 in 5 women with breast cancer would be HER-2 positive, and not all of those would be eligible for treatment, but even so this would be large burden, and use of trastuzumab would probably be bigger than what is usually regarded as affordable.

So great science produces good results that we cannot afford. We need to think outside the box. The patent-protected life of a medicine is 20 years or so, with much of that time taken up by laboratory and clinical research before any sales can take place. The result is a short time to recoup development costs, and the high price we pay for drugs.

Perhaps someone ought to consider whether changing patent laws might smooth the way to our ability to develop and use new therapies. If patent life were shortened, development costs would not be recouped, and research and development would end. Longer patent life may be better. Our clever academic economists should so some sums.

Reference:

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**DVT AFTER KNEE ARTHROSCOPY**

The question about whether to give prophylaxis to reduce the risk of serious DVT depends on how likely DVT is in the first place. After some major orthopaedic surgery, estimates of DVT incidence are quite high, perhaps occurring in four of every five patients. In that case, prophylaxis with low molecular weight heparin would seem to be sensible.

Most, though not all, patients who have knee arthroscopy are relatively young, and deep venous thrombosis is rarely a complication, with more serious pulmonary embolism even rarer. But DVT can have sequelae that are far from pleasant, including painful swellings, ulceration, and in extreme cases amputation.

So what is the DVT rate after knee arthroscopy? A new meta-analysis [1] has put a number on it.

**Systematic review**

This was a single search for English-language studies to the end of 2004, together with examination of bibliographies of relevant articles. For inclusion studies had to be prospective, include patients without antithrombotic prophylaxis, involve universal screening if the lower extremities using diagnostic venography or ultrasound, and involve only arthroscopic knee surgery without ligament surgery or open procedures.

**Figure 1: Size of study and DVT incidence (venography dark symbol, ultrasound light symbol)**

![Figure 1: Size of study and DVT incidence](image)

**Results**

Six studies were found, two using venography (dark symbols in Figure 1), and four ultrasound (light symbols). The average age in these studies was 38-46 years, with more men than women.

Individual results for total DVT incidence ranged from 3.1% to 18% in the studies, and in the 684 patients overall it was 10% (95% confidence interval 8-12%). The venography studies picked up 11 cases of proximal DVT, for an overall rate of 2%. No cases of pulmonary embolism were reported.

**Comment**

Including only studies with prospective screening using trusted methods gives confidence in the results, and while there was variability between the studies, this was only to be expected given their relatively small size. The overall result of a 10% DVT rate is interesting. It is probably too low for prophylactic use of low molecular weight heparin, but too high to be ignored.

Some of the individual studies looked for risk factors, useful for picking those patients having arthroscopy who should receive antithrombotic prophylaxis. Individually they were too small to provide great insight, but those suggested include older age (over 65 years), obesity, smoking, previous DVT, venous insufficiency and use of HRT or oral contraceptives. Not finding any cases of pulmonary embolism means we can be 95% confident that it occurs less frequently than 1 time in 230 cases, which is probably what we know anyway. The actual pulmonary embolism rate after knee arthroscopy is not known with certainty.

Reference:
The foramen ovale is a channel between the atria of the foetal heart allowing blood to flow from the right to the left atrium, which shunts oxygenated blood to the systemic circulation during foetal development. It is not needed in adult life when the lungs are functional, and closes after birth. Or at least it closes most of the time, because defects in the septa between the atria are relatively common, and a significant minority of adults have a patent (open) foramen ovale.

Patent foramen ovale (PFO) is associated with increased risk of stroke. In recent years it has also been associated with migraine. While closing a large PFO to try and prevent stroke might make sense, cardiac surgery to prevent migraine, however bad, is difficult to justify.

This short article examines some of the literature on PFO incidence, and takes a quick look at the current evidence on PFO closure and the effects on migraine.

Finding PFO

There are two main methods. One is to look at the heart directly, usually after death. When patients are alive, the main method is transoesophageal echocardiography (TEE). The first question is whether these two methods give the same answer, and whether they are diagnostically equivalent. The answer [1] is that they are.

Briefly, 35 consecutive patients with prior TEE who died underwent a post mortem examination of the heart. Post mortem PFO was found in 9/35, and TEE picked up the same nine. Moreover, both methods gave the same PFO diameter (Figure 1). We might expect case series using either method to give the same result, therefore.

Figure 1: Patent foramen ovale diameter measured at autopsy and by colour doppler transoesophageal echocardiography

<table>
<thead>
<tr>
<th>Year</th>
<th>Hearts</th>
<th>PFO (%)</th>
</tr>
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<tbody>
<tr>
<td>1897</td>
<td>399</td>
<td>26</td>
</tr>
<tr>
<td>1900</td>
<td>306</td>
<td>32</td>
</tr>
<tr>
<td>1918</td>
<td>1809</td>
<td>29</td>
</tr>
<tr>
<td>1931</td>
<td>4083</td>
<td>25</td>
</tr>
<tr>
<td>1934</td>
<td>500</td>
<td>17</td>
</tr>
<tr>
<td>1948</td>
<td>492</td>
<td>23</td>
</tr>
<tr>
<td>1972</td>
<td>144</td>
<td>35</td>
</tr>
<tr>
<td>1979</td>
<td>64</td>
<td>31</td>
</tr>
<tr>
<td>1984</td>
<td>965</td>
<td>27</td>
</tr>
<tr>
<td>1994</td>
<td>500</td>
<td>15</td>
</tr>
<tr>
<td>TOTAL</td>
<td>9262</td>
<td>25</td>
</tr>
</tbody>
</table>

Table 1: Anatomical studies of patent foramen ovale over the past century

The incidence of PFO in over 9,000 hearts was 25%, in studies going back to 1897 (Table 1). Most studies gave similar results, of about 20-30%. The two most recent [2,3] were interesting for two reasons. A detailed US autopsy study [2] examined 100 normal hearts (50 of each sex) for the first ten decades of life. It found that PFO incidence was similar in men and women, and declined gently with age (Figure 2). It also provided information about PFO size, which was 11 mm or below in all but two of 265 cases, and predominantly 5 mm or less (Figure 3).

Figure 2: Incidence of patent foramen ovale at autopsy in 965 normal hearts, by age

Figure 3: Size of patent foramen ovale at autopsy in mm in 265 hearts
The most recent French study [3] was somewhat different because it examined only hearts from 500 people who died with acquired cardiovascular pathology, mainly coronary artery disease. This study had the lowest PFO incidence of any of the anatomical studies of hearts, at 15%.

A large study involved 1,000 consecutive patients [4] referred for TEE most often to rule out possible cardioembolic sources of stroke, in patients with an average age of 60 years. It also found equal incidence in men and women, and included a review of other TEE studies since 1988 (Table 2). In all these studies combined, with 2,025 patients, the overall incidence of PFO was 10%.

Put simply, then, two methods that ostensibly have equal accuracy provide different results. A possible cause may be the type of patients investigated, with perhaps a lower incidence of PFO in patients investigated with TEE for clinical reasons.

### PFO incidence in migraine

Consecutive patients with migraine with aura (93) participated in a study along with healthy individuals from hospital staff or novice divers (93), and these two groups were similar in age and other characteristics, with about 60% women [5]. Upon examination with TEE, it was found that significantly more of the migraine patients had PFO (47%) than controls (17%). A much larger percentage with moderate, and especially with large shunts, had migraine (Figure 4).

The higher incidence of PFO in patients with migraine with aura confirmed a previous Polish study [6] that investigated 62 patients with migraine with aura, 60 without aura, and 65 controls. Using TEE it found no difference between patients with migraine without aura and controls, but a PFO incidence twice as high in patients with migraine with aura (Figure 5).

### Closing the shunt

Several studies have shown the increased prevalence of PFO and shunting in patients with migraine, and the expectation, therefore, might be that by closing the defect the migraine will be improved. An editorial reviewed six studies (17 to 215 patients) that looked at the effect of PFO closure on migraine, but only one of them, with 17 patients, looked only at migraine. In all, only 205 patients had migraine in a set of mainly retrospective studies, but there was a tendency to see resolution or improvement in quite a high proportion.

As often happens, though, early enthusiasm is tempered by later experience. A large retrospective study of all patients undergoing percutaneous atrial septal defect closures in Oslo was able to include 75 patients with migraine (66% of the total [7]). It found no difference in before and after incidence for migraine with and without aura. In some patients (12/75) migraine disappeared, but migraine appeared for the first time in 10 others.

### Comment

It may all come down to swings and roundabouts. If you ask about migraine disappearance you get one answer. Ask about new migraine, and you get another. Tsimitas [7] gives a number of reasons why linking atrial septal closure with migraine disappearance may be all hype.

- Firstly, there aren’t many patients in these studies.
- Secondly, none is a randomised trial.
- Thirdly, the studies depend on recall, and most are retrospective.
- Fourthly, there was no blinding for patients or carers.
and expectation may have played a part.

- Fifthly, patients undergoing cardiac procedures have lots of medications afterwards, and we don’t know about the effect of those medicines alone or in combination.
- Sixthly, new migraine after septal closure is not confined to the Norwegian study [8].
- Seventhly, completeness of closure does not seem to be associated with migraine relief.
- Eighthly, apart from septal closure and postoperative medicines, there are other things going on in these studies that have not been controlled for, so there is no evidence for causality even if there were evidence for a link.
- And ninthly, someone has to explain why prevalence of PFO is equal between the sexes, while migraine occurs three or four times more frequently in women.

Healthy scepticism should be the watchword here. On the basis of current evidence, it would hardly be wise to have cardiac surgery for migraine, when even in the best hands there is always the risk of something going seriously wrong.

Let’s keep an open mind, but bearing in mind what Bertrand Russell said: the trouble with the world is that the stupid are cocksure and the intelligent are full of doubt.

BARRETT’S OESOPHAGUS INCIDENCE

Barrett’s oesophagus is where squamous epithelium is replaced with columnar epithelium. Probably caused by prolonged reflux of acid into the oesophagus, it is a major risk factor for oesophageal cancer, increasing the risk by 30-100 fold. The incidence of oesophageal cancer is rising, and a study [1] tells us that Barrett’s incidence is also rising.

Study

This was an integrated database study from Holland, based on over half a million patient records maintained since 1992. Patients contributing data between 1996 and 2003 inclusive involved 386,000 patients for 1.3 million person years of follow up. The database gave details of patients having upper gastrointestinal endoscopy, and the results of the endoscopy. Incidence was calculated by dividing the number of cases by the population at risk.

Results

There were 491 definite or probable cases of Barrett’s oesophagus after medical record review. The incidence of Barrett’s oesophagus for each 100,000 patient years and per 1000 endoscopies is shown in Figure 1. The 10-year risk of being diagnosed with Barrett’s oesophagus rose with age from 0.1% in the early 30s to almost 1% at 70 years. There were more men (61%) than women, and the mean age at diagnosis was lower (59 years) in men than in women (66 years).

Adenocarcinoma of the oesophagus was detected in 51 patients over the period, 76% in men, at a mean age of about 70 years. The incidence increased threefold over the period, and was 6 (95% confidence interval 3-10) per 100,000 person years in 2002. It could be higher, because some cases of unknown type were omitted.

References:

Comment

Obesity and acid reflux are two major risk factors for Barrett’s oesophagus, and these findings are likely to be another manifestation of the fattening of populations. Endoscopy was largely driven by guidelines for reflux, and not all patients with Barrett’s oesophagus have reflux, so the actual incidence could be higher.

Reference:
Grapefruit seed extracts
and health

Back in 2000, Bandolier 73 carried a brief account about how it had looked for trials of grapefruit seed extract and health, and had failed to find any. Grapefruit seed extract (from here on in abbreviated to GSE) is promoted because it kills harmful micro-organisms, based on laboratory tests that demonstrate antimicrobial effects. What was apparent was that manufacturing GSE concentrated antimicrobial preservative chemicals used on grapefruit, and it was likely that it was those chemicals that had the antimicrobial effect.

That small article has attracted almost more email correspondence than any other, so for a bit of peace and quiet, here’s an update.

GSE and its effects on health

Figure 1 shows the evidence. No, it isn’t a misprint, it is a box filled with nothing. Bandolier has searched again for studies that demonstrate that eating GSE in any form benefits health. There is none we could find.

Now we might have missed hundreds of good quality randomised trials (a form of publication bias in reverse), but we don’t think so. If anyone knows of good evidence, let us know. But we don’t want anecdotal accounts of miraculous cures of sick cats, because sick cats often do quite well on their own.

GSE and biocides

The first reference we found was in a Japanese journal [1], in which three compounds were found, two of which were identified as methyl-p-hydroxybenzoate and 2,4,4’-trichloro-2’-hydroxydiphenylether (triclosan). Commercial grapefruit seed extract was quite different from grapefruit seeds, which did not contain these chemicals.

In the second, analysis of six commercial grapefruit seed extracts [2] showed five had antimicrobial properties, and were active against a strain of Candida. In all extracts with preservative substances contained. Pharmazie 1999 54: 452-456.

The US Department of Agriculture has also been doing some investigation of commercial GSE. Their first study [3] found benzethonium chloride. In two GSE samples, the benzethonium chloride amounted to 8% by weight of the GSE sample, so this was no trace constituent. A more recent study [4] found benzyldimethyldecdyramonium chloride, benzyldimethyltetradecylammonium chloride, and benzylidimethylhexadecylammonium chloride, commonly known as benzalkonium chloride.

For the avoidance of doubt, these chemicals are not made by grapefruit. They are synthetic chemicals added to the grapefruit seed extract at some stage. Benzethonium chloride is commonly used in cosmetics and other topical applications, and benzalkonium chloride is widely used as an ingredient in cleaning and disinfectant agents.

Comment

Step back a moment from any prior thinking you may have about natural remedies or medicines, about alternative or conventional medicine. Which of us is likely to think that we or a loved one is going to be better off with a nice dose of drain cleaner? Yet right now, the one thing we know is that commercial GSE contains powerful chemicals, but we don’t know which ones in which extract, or how much is there. It is a bit like an addict mainlining with strychnine rather than heroin because it is a white powder. The evidence is that GSE without drain cleaner kills no bugs [2].

Yet journalists peddle this stuff in their papers or online all the time. Try GSE for its natural antibacterial action, they say, taken in by the guff and unwilling to do any research. Wake up and smell the drain cleaner.

If journalists want to give safe advice to people who want natural antimicrobials, why not suggest a spoonful of honey? We know honey contains antimicrobial agents, and that it prevents and treats infected wounds, both because of its hyperosmolar nature, and because of these antimicrobials. There is no trial evidence that eating it does any good, but (anecdotally) people with MRSA have cleared it from their system by eating honey. And if the honey were eaten on a slice of wholegrain bread, that would reduce the risk of cancer by about half, as mentioned in Bandolier 53.

References:


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Bandolier 142