Treatment of Patients Suffering from Constipation with Eucarbon® herbal Tablets

Open, multicenter, prospective, non-interventional study

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Abstract:
In an open, multicenter, prospective, non-interventional study (NIS) efficacy and safety of Eucarbon® herbal tablets, containing senna leaf, rhubarb extract, and wood charcoal, were investigated in 50 patients suffering from constipation. After two weeks treatment, all 50 patients were available for evaluation, whereby the following questionnaires and criteria were used: Number of complete spontaneous bowel movements (CSBM) per week [main efficacy criterion], modified Clinical Global Impressions (CGI), improvement of problems and complaints with bowel movements (regarding to Rome-III criteria), global assessment of efficacy / therapeutic effect by physician and patient, body weight. Visits took place before treatment, after one week and after two weeks of treatment. The majority of patients took 3 x 2 tablets. The mean number of CSBM was nearly doubled. All major symptoms and complaints, like abdominal pain, bloating, feeling of incomplete evacuation, straining necessary decreased significantly during treatment. The medication was tolerated very well.

In conclusion the efficacy and safety of the natural product Eucarbon® herbal tablets in the indication constipation could be confirmed.

Keywords:
Rhubarb, senna, non-activated charcoal, non-interventional study, Eucarbon® herbal

Introduction:
Constipation refers to bowel movements that are infrequent or hard to pass. Constipation is a common cause of painful defecation. The normal frequency of evacuations varies individually from three times daily to three times a week. Constipation per se is diagnosed if no bowel movements occur for three days or more, and if this irregularity persists for longer than six days. Constipation is not an illness, but a symptom with many causes, which are of two types: obstructed defecation and colonic slow transit (or hypomobility). Acute constipation starts suddenly and lasts for a few days.

Chronic constipation is one of the most common complaints in clinical medicine. It is a rising problem in modern society affecting approximately one of five adults in industrialized countries. Chronic constipation is defined as the delayed evacuation of dry, hard stools [MUTSCHLER] or the passage of small hard faeces infrequently and with
difficulty [FALLON]. Because constipation is a symptom, not a disease, effective treatment of constipation may require first determining the cause.

The most common causes are associated with nutritional factors such as the consumption of food with poor dietary fibre content, which results in insufficient filling of the intestine. Furthermore, intake of readily absorbed food with a reduced water-binding capacity or the lack of exercise may lead to constipation. Other causes include factors related to organ dysfunction or organ damage including gastro-intestinal disorders, changes in the intestinal wall (due to a tumour or chronic inflammation e.g.), metabolic and endocrine disorders (diabetes mellitus e.g.), functional and organic disturbances of the nervous system, such as Parkinson’s disease, or may be caused by the side-effects of drugs such as analgesics, antidepressants, antispasmodics or sedatives [WALD].

For long times „constipation“ was not defined clearly in professional circles. It was in 1999 when in Rome during a specialists' conference definitions were agreed which nowadays are known as „Rome-criteria“. In the course of time these regulations have been modified insignificantly and are valid today as ‘Rom-III-Criteria’. By this definition chronic constipation is understood as a combination of different symptoms. The Rome Criteria for chronic constipation [DROSSMAN] require at least two of the following symptoms for 12 weeks or more over the period of six months:

- Straining with more than one-fourth of defecations
- Hard stool with more than one-fourth of defecations
- Feeling of incomplete evacuation with more than one-fourth of defecations
- Sensation of anorectal obstruction with more than one-fourth of defecations
- Manual maneuvers to facilitate more than one-fourth of defecations
- Fewer than three bowel movements per week

The management of constipation extends well beyond the use of laxatives. There is a general agreement in selecting therapeutic strategies for treatment of constipation. Non-surgical treatment can be separated into: dietary approaches such as fibre supplementation, behavioural approaches such as habit training, contingency management, and biofeedback, exercise as well as pharmacological approaches.

The aim of laxative therapy is to achieve comfortable defecation, rather than any particular frequency of evacuation. Although most laxatives are not very palatable, oral laxatives should be used whenever possible. The choice of laxative depends on the nature of the stools, the cause of the constipation, and acceptability of the patient.

When choosing laxatives, knowledge of the main mechanism of their action is needed. Many of the softeners increase stool bulk and lead to reflex stimulation of peristalsis, and, similarly, the peristalsis stimulators enhance intestinal fluid secretion and therefore improve stool consistency [WALD].

One since decades internationally used medication in the indication constipation is Eucarbon®, a charcoal-sennosides combination which is indicated for the relief of the symptoms of constipation and general gastrointestinal disorders, which was already developed in 1909 and is since than available; it is a unique medicine out of natural components known since centuries. The original composition contains also purified sulphur. The newer formulation Eucarbon® herbal tablets has the same unchanged composition, but without sulphur. Eucarbon® herbal tablets contain only vegetable and
natural active ingredients and are produced with up-to-date production methods in accordance with GMP-standards. Eucarbon® herbal stimulates the entire digestive system, increases colonic motility, has a mild laxative and spasmolytic effect, relieves gas pain and can also be regarded as a detoxifying agent (mild adsorbent). In the unique combination of this preparation the proven and generally accepted effects of the single ingredients have additional beneficial effects – presented in a standardized dosage form.

Aim of this study was to gain further knowledge on the daily use practice and safety of Eucarbon® herbal tablets in patients suffering from constipation. As it is known that eating and living habits as well as traditions are different all over the world and vary from country to country it is important to evaluate and understand if a “European composition” for a herbal drug known and established for more than 100 years will have the same profile of efficacy and tolerance in an Asian country, where the population has quite different nutritional behaviour and culture.

The study design was a non-interventional, open, perspective, multicenter study (NIS) which was planned, conducted and evaluated by the current state of scientific knowledge. The patients were informed and asked for written consent by the treating physician. National laws and regulations regarding patient information, data protection, and documentation were respected and obeyed. An Institutional Review Board has been consulted which had approved the study.

Methods

This study aimed to proof the well-known safety profile of an approved drug under daily practice conditions. Main efficacy criterion was the increase of the frequency of complete spontaneous bowel movements (CSBM) per week compared to base-line [anamnestic data] with a minimum of seven days treatment. Secondary end-points included course and intensity of specific symptoms like abdominal complaints, hard stool, feeling of incomplete evacuation, bloating. All data of the examinations and treatment were documented in prepared case report forms (CRFs). Physicians who participated in this study had to be well versed in diagnostics and treatment of gastro-intestinal diseases.

As a NIS in this study the medicinal product had to be prescribed in the usual manner in accordance with the terms of the marketing authorization. No additional diagnostic or monitoring procedures were applied to the patients and epidemiological methods were used for the analysis of the collected data. The treatment could be finished at any time at the decision of the physician if the situation, course of treatment, or illness required.

Generally the individual time of treatment and observation of a patient was two weeks. In particular it depended on the decision of the treating physician regarding the course of treatment, and the individual situation of the patient.

The planned observation time for the whole study population was from May 2013 to October 2014. Included in this study should be men and women with the diagnosis „constipation“ (acute as well as chronic constipation) in the age of 18 to 70 years, who were out-patients in practices of general practitioners or specialists for internal medicine or were treated in hospitals for internal medicine in Malaysia.

Parameters for the assessment of a successful treatment with Eucarbon® herbal were: number of complete spontaneous bowel movements (CSBM) per week, clinical findings,
problems and complaints with bowel movements (regarding Rome-III criteria), modified Clinical Global Impressions Scale (CGI) [GUY] regarding the severity of disease, global assessment of the efficacy / therapeutically effect by the treating physician and patient. Each patient received Eucarbon herbal tablets, where the recommended dosage was 3 x 2 tablets/day. Active ingredients in Eucarbon herbal tablets (Manufacturer: F.TRENKA, Vienna, Austria) are: Fol. sennae (Senna Leaf) 105,00 mg; Extractum Rhei (Rhubarb Extract) 25,00 mg; Carbo Ligni (Wood Charcoal/Vegetable charcoal) 180,00 mg, and two additional relevant excipients: Peppermint oil 0.50 mg, and Fennel oil 0.50 mg.

Results

During the time period of July 2013 to February 2015 the study was performed in eight gastroenterological specialist clinics in Malaysia, where 1 to 18 out-patients were treated per center with Eucarbon® herbal tablets. 25 patients suffered from acute constipation (50%), 19 from chronic constipation (38%), 4 from abdominal colics, and 2 from abdominal discomfort / colics. Completely documented case report forms are available for 50 patients: male: 26, female: 24 in the age of 7 – 82 years (mean: 37.34; median: 38 years), a body-height of 110 – 176 cm (mean: 167.69; median: 160 cm), and a body-weight at the inclusion day of 45 – 95 kg (mean: 63.24; median: 62 kg).

The mean number of spontaneous bowel movements/defecations in the week before inclusion in the study was 2.8 (with a range of 0 to 7 spontaneous defecations). The mean “complaints with bowel movements” (regarding Rome-III criteria) before treatment (assessed by a scale from “0 = no complaints or seldom”; “1 = minor, easy to resist”; “2 = affecting”; “3 = strongly affecting” to “4 = heavily”) was 1.98.

A total of 17 patients took different kinds of laxatives before entering the Eucarbon® herbal study: most frequently: Dulcolax, Senekot, “herbal treatment”, Buscopan, and “enema”. Most commonly reported comorbidities / risks were piles/hemorrhoids (10 pats), smoker (8), alcohol (2), diabetes mellitus (2 pats). 20 pats. (40%) lamented occasionally bloating, 14 (28%) seldom, and 12 (24%) frequent bloating.

All patients completed the study; there was no premature interruption of treatment or drop-out. Most patients (n = 21, 42%) finished the study as recommended after 2 weeks (mean: 15,1; median; 15 days). In none of the 50 patients any clinical findings / abnormalities / drug related complaints were reported.

At the beginning of the study in 34 pats. (68%) the tablet dosage of Eucarbon® herbal recommended by the Investigator was 6 (3 x 2) per day, in 8 pats. (16%) 3 tabs. (3 x 1) per day. The dosage of Eucarbon® herbal during the two weeks treatment was increased in 4 pats. (from 4 to 6 tabs/day), decreased in 3 pats. from 6 to 4 and 3 resp., and unchanged in 43 pats (86%).

Fig. 1 shows the mean values of spontaneous bowel movements during the course of the treatment. The mean values increased from 2.8 before to 4.37 (1.7 – fold) after one and 5.28 (1.9 – fold) after two weeks of treatment.
Fig 1: Quantity of spontaneous defecations (CSBM) before and under treatment.

Additionally the quality of different symptoms of defecations was assessed by a scale system from zero to four ["0 = never/seldom"; "1 = sometimes"; "2 = often"; "3 = mostly" to "4 = always"] before and after treatment (see Tab. 2).

Fig. 2: Quality of defecation - before and under treatment

As result in fact all five typical symptoms were improved: more "subjective symptoms" like "feeling of incomplete evacuation" (by 78%), "sensation of anorectal obstruction" (by 71%) as well as more "objective symptoms" as "hard stool" (by 69%), "straining necessary" (by 77%) (see Fig. 2). The least improvement was documented regarding the criterion "manual maneuvers to facilitate" (by 39%) which per se is a very rare measurement with low starting value and thus can only be improved to a lesser extent.
The complaints with bowel movements (regarding Rome-III criteria), before and after treatment assessed by a scale [from “0 = no complaints or seldom”; “1 = minor, easy to resist”; “2 = affecting”; “3 = strongly affecting” to “4 = heavily”] decreased by 73.2% from 1.98 to 0.53.

<table>
<thead>
<tr>
<th>Degree of complaints</th>
<th>Before Treatment Number of Patients [n = 50]</th>
<th>After Treatment Number of Patients [n = 50]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0 (0%)</td>
<td>23 (46%)</td>
</tr>
<tr>
<td>1</td>
<td>12 (24%)</td>
<td>19 (38%)</td>
</tr>
<tr>
<td>2</td>
<td>27 (54%)</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>3</td>
<td>11 (22%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>n.a.</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Mean:</td>
<td>1.98</td>
<td>0.53</td>
</tr>
<tr>
<td>Decrease:</td>
<td></td>
<td>73.2%</td>
</tr>
</tbody>
</table>

Tab. 1: Complaints with bowel movements before and after two weeks treatment.

Furthermore one very distressing symptom - bloating – could be very clearly improved: from a mean value of 1.91 before treatment to 0.28 after two weeks treatment – a decrease of 85.34%.

Fig. 3: Symptom Bloating - Before and after treatment, in categories: “0 = no”; “1 = seldom”; “2 = occasionally”; “3 = frequent”

Tab. 2 shows the assessment with the modified Clinical Global Impressions Scale (CGI) regarding the severity of disease at time in the categories 0 - 6: “0 = normal, not at all ill”; “1 = patient is borderline ill”; “2 = mildly ill”; “3 = moderately ill”; “4 = markedly ill”; “5 = severely ill” to “6 = patient is extremely ill”. A mean decrease of 72.2% (from 1.44 to 0.4) could be documented.
<table>
<thead>
<tr>
<th>Category</th>
<th>Number of Patients [n = 50]</th>
<th>CGI before</th>
<th>CGI After 2 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10 (20%)</td>
<td>35 (70%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16 (32%)</td>
<td>11 (22%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>18 (36%)</td>
<td>3 (6%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4 (8%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Mean:</td>
<td>1.44</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Decrease:</td>
<td></td>
<td>72.2%</td>
<td></td>
</tr>
</tbody>
</table>

Tab. 2: Clinical Global Impression Scale (CGI) - Before and after treatment

One interesting side benefit is the loss of weight: more than half of the patients lost weight [between 0.5 to 5 kg] in mean 1.4 kg in only two weeks. 30% kept their weight and in 6 patients (12%) a gain in weight of 0.5 to 1 kg was documented.

The final global assessment of the therapy with Eucarbon® herbal by the investigator after the two weeks treatment regarding efficacy and tolerance/safety was prevailingly as “very good” (see Fig. 4).

Fig. 4: Final global assessment of the efficacy of the therapy by the investigator after two weeks treatment

In 41 pats (82%) the investigator gave the recommendation for the continuation of Eucarbon® herbal intake after the two weeks treatment, in 8 of them (16%) in a reduced dosage.
Discussion

Eucarbon® was developed in 1909 by the pharmacist Mag. F. Trenka and by Prof. Dr. W. Pauli who composed a unique medicine out of natural components known since centuries. Eucarbon® tablets contain only vegetable and natural active ingredients and are produced with up-to-date production methods in accordance with GMP-standards. Eucarbon® stimulates the entire digestive system, increases colonic motility, has a mild laxative and spasmylytic effect, relieves gas pain and can also be regarded as a detoxifying agent (mild adsorbent). The overall tolerability and safety of Eucarbon® is worldwide known and documented for more than one century. Using Eucarbon® as a drug of choice in constipation has never been associated with severe or even life-threatening adverse reactions. In the usual dosage regime, i.e. at the recommended doses, Eucarbon® does not even show preparation-related side effects, neither in the daily practice nor in the studies performed. There are no preparation-specific contra-indications known neither findings on drug interactions nor any restrictions on the ability to drive or to operate machinery. Because of concerns of some Regulatory Authorities regarding sulphur as active ingredient, Eucarbon® herbal has been developed which is as well a combination of anthranoid drugs (senna and rhubarb), and the mild adsorbent vegetable charcoal (carbo ligni) in the same composition as Eucarbon® but without sulphur. Eucarbon® herbal is as well used as a medicinal product with mainly laxative effects. The action of the preparation is due to the content of vegetable charcoal and the stimulatory action of anthraquinones. The use of vegetable charcoal, rather than activated charcoal, avoids the significant drug binding of anthraquinones as well as potential interactions. The adsorption properties of carbo ligni are regarded for the effect to cure complaints due to intestinal gases [HÜBNER]. This adsorbent activity of carbo ligni, although definitely lower compared to activated charcoal, has been extensively studied during the last 30 years. It could be demonstrated that carbo ligni adsorbs many chemical entities, but does not inhibit the release and efficacy of the anthrachinone glycosides from Eucarbon® / Eucarbon® herbal. The detoxifying effect has also been studied and shown in in-vivo studies by various study groups [SCHMIDBAUER].

Long-time experience and clinical studies have demonstrated that patients taking Eucarbon® for one or two weeks get relief of abdominal swelling and of dyspeptically troubles. The action of Eucarbon® is gradual, mild and prolonged. This determines its value. Eucarbon® is a very well-tolerated product. As the effect of sulphur is mainly disinfectant – and the composition of the main active ingredients is the same one in Eucarbon® and Eucarbon® herbal tablets the long-term experience regarding safety and efficacy is transferable from Eucarbon® to Eucarbon® herbal tablets, which is also accepted by the Authorities. Thus in the following the data gained with Eucarbon® tablets are used as evidence for Eucarbon® herbal as well.

Eucarbon® belongs to the group of medicines possessing mild laxative and purgative properties and having a wide spectrum of pharmacological effects. It is not only a mild laxative but also a digestive regulator. At low dosage of 1 to 3 tablets per day, Eucarbon® exhibits its adsorption power, at higher dosages of 4 to 6 tablets per day Eucarbon® acts as an adsorbent and mild laxative.

In case of constipation the herbal laxative have the effect, within six to eight hours, of softening the faeces, thereby facilitating defecation, as their action takes place in the colon.
In a couple of clinical studies the efficacy of Eucarbon® regarding constipation could be proven. Breier performed an open clinical study with 102 patients in a general practice. Eucarbon® was found to be effective in over two thirds of the patients treated at a dose of (usually) two tablets daily (or higher doses – up to six tablets daily – in 31 subjects). The patients’ age ranged from 35 – 90 years (mean 71 years). The observation period was one week. The assessment of symptomatology was focused on constipation, abdominal distension, colicky abdominal pain, nausea, flatulence, vomiting, diarrhoea and insomnia. The following five symptoms were significantly improved by treatment with Eucarbon® during the study: constipation, abdominal distension, colicky abdominal pain, nausea and flatulence, p-values ranged from <0.01 to <0.001 for the individual symptoms. There were no reports of side-effects or of intolerance to the medication [BREIER].

Feruglio performed an open evaluation with 31 in-patients admitted to his hospital in Trieste, Italy with general medical complaints, suffering additionally from intestinal complaints, constipation or bellyache, were treated with Eucarbon® at doses of 3 – 6 tablets per day for 6 to 26 days. The patients’ age ranged from 48 to 96 years (mean age 68). Best results were obtained in patients with persistent constipation. The effects of Eucarbon® were found to be satisfactory, especially in cases of constipation with pronounced meteorism, there were no reports of side effects at this dosage [FERUGLIO].

In a drug-monitoring study of Hübner and Alken, the efficacy and safety of Eucarbon® tablets were investigated in patients suffering from constipation, especially those with spasmodic complaints. After the 12-week treatment period, 61 patients were available for analyses, whereby the following questionnaires were used: global assessment for efficacy and safety/tolerance, modified Clinical Global Impressions Score (CGI), and modified Francis Score (IBS-Score). The majority of the patients took 3x2 tablets daily. All major symptoms and complaints like abdominal pain, altered frequency of stool, flatulence, hyperperistalsis, tenderness on pressure, tympanitic resonance decreased during treatment. The medication was very well tolerated [HÜBNER and ALKEN].

The aim of this study, reported here, was to gain further knowledge on the daily use practice and safety of Eucarbon® herbal tablets in patients suffering from constipation in a setting which has not been not studied so far. Main efficacy criterion was the increase of the frequency of complete spontaneous bowel movements (CSBM) per week compared to base-line [anamnestic data] with a minimum of seven days treatment. The secondary end-points included: clinical findings, problems and complaints with bowel movements (regarding Rome-III criteria), course and intensity of specific symptoms like abdominal complaints, hard stool, feeling of incomplete evacuation, bloating, as well as the modified Clinical Global Impressions Scale (CGI) regarding the severity of disease and the global assessment of the efficacy / therapeutically effect by the treating physician and patient.

As an overall result of this study the treatment with Eucarbon® herbal tablets can be regarded as very successful as the main as well as the secondary efficacy criteria resulted in very good values. All patients completed the study, no premature interruption of treatment or drop-out occurred. The controls were performed in most patients after a mean of 15 days of treatment. Only two patients took additional laxatives for few days – thus not influencing the overall results. More than half of the patients changed their eating habits and eat more fruits, vegetables, fiber diet and/or drunk more fluids. Which may have some effect, but if - only a minor one, as the other results speak for themselves. The remarkable decrease in bloating e.g. cannot be explained by taking
more fibers – in contrary. More than two thirds of the patients took the recommended dosage of 3 times two tablets daily which obviously has proved to be the right dosage for the majority of patients with constipation. In seven cases a dose adjustment was recommended by the investigator, leading to a successful progression of treatment during the further course of the study.

The main efficacy criterion - increase of the frequency of CSBM per week – is successfully fulfilled by an increase of 1.7-fold after the first, and 1.9-fold after the second week of treatment [from 2.8 to 4.4 and 5.3 CSBM per week – which is nearly doubling]. Bloating as a particularly harmful symptom decreased dramatically from 1.9 [“occasionally”] to 0.28 [which is near to “0 = no”]. The complaints with bowel movements changed from a mean of 1.98 [on the scale from 0 to 3] to 0.53 – which is a decrease of more than 73%. Similar values are obtained with the modified Clinical Global Impression Scale: from a mean of 1.44 to 0.4, a decrease of about 72%. Regarding the quality of defecations an overall improvement between 70% and 78% was found concerning the symptoms hard stool, necessity of straining, feeling of incomplete evacuation and sensation of anorectal obstruction – all symptoms which affect the patients in their daily living heavily. In the criterion “manual maneuvers to facilitate” there was only an improvement of about 40% which is easily to explain by the very low initial value of only 0.28 scale points which is practically zero – thus can hardly be improved – but in fact could be to 0.17.

One very interesting side benefit is the loss of weight: more than half of the patients lost weight [between 0.5 to 5 kg] in mean 1.4kg in only two weeks. 30% kept their weight and in 6 patients (12%) a gain in weight of 0.5 to 1kg was documented.

The overall final global assessment of the therapy by the investigator resulted in 66% good and very good for the efficacy [and 34% regarded as satisfying or sufficient] – which means that in all patients the treatment was judged as convincing. There were no side effect reports nor safety concerns, as the tolerance was described in 74% of the patients as good and very good and in the remaining 24% as satisfying or sufficient. Values which are corresponding to the patients’ overall judgment [including efficacy and safety] which results in 98% for notable to very good effects.

Summing up - the treatment with Eucarbon® herbal tablets in the recommended dosage lead to the desired effects - increase of CSBM per week, a remarkable decrease in complaints and an improvements of the quality of defecations with a convincing safety profile - thus delivering the proof of being a successful therapeutically principle in the treatment of constipation also in an Asian population.

Although Eucarbon® herbal is mainly indicated in the treatment of constipation and indigestions, in patients taking colon motility hampering drugs like morphines, and in bedridden patients it is also successfully used in radiology in the preparation for improvement of X-ray and/or ultrasonic abdominal investigations [El MRINI, NICOLOVA, OKASHA, SCHMIDBAUER].

But as Eucarbon® possesses unique properties and is furthermore a valuable tool as well in general digestive disorders with special regard to the indication irritable bowel syndrome (IBS) [HEINZ, HÜBNER and MOSER, KREIJS]. In all studies cited efficacy in the indications investigated and safety could be proven. The medication was generally tolerated very well.
Because of its good tolerance and lack of drug-drug interactions Eucarbon® and Eucarbon® herbal tablets seem to be especially appropriate for the elderly and for long-term treatment, e.g. in heart patients to be used to stop or reduce flatulence and hence diminish the pressure on diaphragm – thus causing heart rate to revert to normal [FARR].

One special point which should be discussed regarding the composition of Eucarbon® herbal – is the assumption of a potential toxicity of senna.

It was in 1984 when Dobb and Edis published a number of case reports concerning potential senna toxicity including coma and neuropathy after ingestion of a senna-combination laxative and hepatitis after long-term use of the plant [DOBB and EDIS]. In the publication of Siegers et al.: "Anthranoid laxative abuse - a risk for colorectal cancer?" in 1993, it was published that the use of anthraquinone containing drugs as laxatives with aloe, cascara (Senna), frangula and rheum might be associated with the development of Pseudomelanosis coli, and further on maybe with adeno-carcinoma and colorectal carcinoma [SIEGERS].

But consecutive international reports on clinical studies, reviews, publications of Health Authorities and at least a lot of animal studies revised these results: In the “Melbourne colorectal carcinoma study” by Schumann in 1993, being the same year as the publication of Siegers et al., this group has documented that the use of laxatives, mainly containing anthraquinone derivatives has to be regarded as save [SCHUMANN]:

- The commercial laxative use was similar in 685 colorectal cancer patients and 726 age and sex-matched community based controls
- Previous use of anthraquinone laxatives and of phenolphthaleine containing laxatives was not associated with a risk of colorectal cancer.

The scientific group around Nusko et al. published in 1997 their report "No risk of colorectal neoplasm after long-term use of anthranoid laxatives" [NUSKO] where it was also stated: “There was no statistic significant risk of anthranoids’ use for the development of colorectal adenoma or carcinoma. Nor were there any differences between patient and control groups in terms of duration of the intake (maximal 20 years). Nor did microscopic Melanosis coli show any significant risk for the development of adenoma or carcinoma.”

On the contrary, in the literature many publications and issues can be found to prove the use of anthranoids and derivatives as anticancer agents [DUNN and GOA].

Wisemann et al. showed in their publication the antitumor effect of the anthraquinone mitoxantrone in prostatic cancer. The antineoplastic agent mitoxantrone in combination with a corticosteroid (either prednisone or hydrocortisone) has shown clinical efficacy as palliative treatment for a proportion of patients (about 35 to 40%) with hormone-resistant advanced prostate cancer [WISEMANN].

In the U.S. Department of Health & Human Services National Institutes of Health Livertox Database it is stated, that the use of Senna in the recommended doses for a limited period of time has been associated with few side effects, most of which are mild and transient and related to its laxative action. With longer term and higher dose use of senna, however, adverse events have been described including several cases of clinically apparent liver damage. The time to onset of liver damage was usually after 3 to 5
months of use, and the pattern of serum enzyme elevations was hepatocellular. The liver damage was usually mild-to-moderate in severity and resolved rapidly with discontinuation. Immunoallergic features and autoimmune markers were not present in the published cases [LIVERTOX DATABASE].

The MCA report "Safety of Herbal Medicinal Products" published in July 2002 [MCA] mentioned for rhubarb and senna as potential adverse events only “purgative, irritant to GI tract” – thus known effects - but recommended to avoid non-standardised preparations during pregnancy. Thus the excellent safety of these drugs could be confirmed.

The European HMPC ASSESSMENT for Senna comes to the result: “Provided that the correct dose and duration of administration and the advices given in the SPC are followed, senna can be regarded as a safe and effective medicinal plant for the short-term use in cases of occasional constipation. In this indication the benefit/risk ratio is positive.” [EMEA]. Thus sufficient studies are published in the literature and evaluated by US and European Agencies to prove the safety of anthranoids and the anticancer properties of anthranoid derivatives - for short time usage in the recommended dose range. Never the less a potential side-effect in case of long-term use - which is not recommended – is the possible loss of electrolytes which might give problems if digitalis drugs are used.

In fact the excellent tolerance of Eucarbon® might also be due to the special combination of senna and rhubarb. It seems possible that the composition reduces furthermore potential side effects arising from senna leaf, an action which would be typical for phytopharmaceutical agents.

Résumé:

The overall tolerability and safety of Eucarbon® is worldwide known and documented over one century. Using Eucarbon® as a drug of choice in constipation has never been associated with severe or even life-threatening adverse reactions. A combination of plant laxatives such as Eucarbon® herbal constitutes appropriate therapy in clinical practice for the treatment of constipation – not only in terms of principal efficacy and safety, but also as regards administration of treatment. One important point is that people very easily can modify and adapt their individual dose and therefore prevent potential stronger side effects that might be expected due to its content of anthraquinones. And benefit to a high degree that Eucarbon® herbal works as a natural intestinal regulator with a unique twofold action as an agent against mild forms of diarrhoea, an adsorbent and mild laxative as documented in this study.
Literatur


