HB 1717

Testimony Presented to

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Professional Licensure Committee

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By:

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Good morning, Rep. Harhart, and distinguished members of the Professional Licensure Commrttee. I am pleased to be here today to testify in favor of HB 1717. My name is Dr. Tim Birdsall, and I am a Naturopathic Doctor, and Vice President of Integrative Medicine at Cancer Treatment Centers of America (CTCA). I completed my undergraduate degree at Grace College in Indiana, received my Doctor of Naturopathic Medicine degree (N.D.) from Bastyr University in 1985, and am currently licensed as a Naturopathlc Physician in both Washington State and Arizona.

Cancer Treatment Centers of America owns and operates cancer hospitals in Illinois, Oklahoma, Pennsylvania and Arizona, as well as an outpatient cancer center in Washington State, CTCA has incorporated Naturopathic Doctors into our facilities since 1998, and today evety patient in our facilities sees a Naturopathic Doctor as a part of their care team.

Medical training for Naturopathlc Doctors is comprehensive and scientifically rigorous. Following a typical pre-medicine undergraduate curriculum, students of naturopathic medicine enroll in an accredited, 4-year naturopathic medical school and receive training in both the basic medical sciences, such as anatomy, physiology, biochemistry and histology, and the clinical sciences, studying the diagnosis and treatment of disease, pharmacology, and the therapeutic use of natural and pharmaceutical products. Naturopathic Doctors diagnose patients using the same basic techniques as those used by any physician – thorough histoy-taking, comprehensive physical examination, and appropriate laboratory tests and imaging studies. Naturopathlc docrors refer patient to specialists when those skill sets are needed for quality patient care.

Cancer is a complex disease, and cancer patients are often very complex medically. Our patients at Cancer Treatment Centers of America, for example, have an average of between 6 and 7 major medical co-morbidities, such as diabetes, hypertension, or heart disease, in addition to their cancer. Just to be clear, natural products alone are almost never appropriate treatment for cancer, and the patients at CTCA receive state-of-the-art conventional cancer care, to which naturopathic care is an adjunct. Not infrequently, patients come to us taking dozens of natural products at the same time they are undergoing chernotherapy or radiation treatment. While many of these products may be beneficial, for any individual patient situation, some may be inappropriate, ineffective or even clearly contraindicated A study I helped conduct at CTCA showed that fully 25% percent of patient combining herbal products with chemotherapy were taking combinations which were contraindicated.[1]

In order to appropriately advise patients with complex diseases on which natural products might be useful, and which might be harmful, the Naturopathic Doctor must draw upon a deep understanding of the pathology of the disease, the pharmacology of medications or other conventional treatments which the patient is receivrng, and the biochemistry and physiologic impact of natural products. Let me give just a couple of specific examples. St. John's Wort is an herb which has been shown to have some benefit in mild to moderate depression, a condition which understandably affects many cancer patients. Unfortunately, St. John's Wort also is a potent inhibitor of the microsomal enzyme system CYP 3A4. This enzyme system is used by the body in the metabolism of approximately 50% of all pharmaceutical drugs. One study looked at the impact of combining St. John's Wort with the chernotherapy drug irinotecan, frequently used in colon cancer. The researchers found that the herb reduced the level of the drug in the body by 42%, likely rendering it ineffective in treating the cancer.'

Another herbal product, curcumin, from the spice turmeric, has a wealth of data suggesting it may be useful in certain cancers. However, research has also shown that curcumin inactivates a substance known as SAPK (Stress-Activated Protein Kinase). Certain chemotherapy agents, such as doxorubicin and cyclophosphamide, commonly used in treating breast cancer depend on an intact SAPK pathway in order to kill cancer cells. While curcumin may be a useful herb in some situations, combining it with doxorubicin or cyclophosphamide may well reduce the effectiveness of the chemotherapy.'

Integrating Naturopathic Doctors into care at Cancer Treatment Centers of America has improved patient care. We have been able to document, for example, that patients with cancer of the pancreas, a highly fatal disease, who utilize naturopathic interventions have significantly lower levels of both pain and fatigue.[4]

Because three of the five locations where Cancer Treatment Centers of America operates facilities are in states which do not license Naturopathic Doctors, CTCA has been held up as an example of why licensing of Naturopathic Doctors is unnecessary. Nothing could be further from the truth. First, as I have already mentioned, licensing statutes are necessary to establish minimum educational standards for nafvropathic doctors. Second, failure to license Naturopathic Doctors results in unnecessary duplrcation of services for patients, since without licensure, NDs are unable to establish a diagnosis, or order lab tests or other diagnostic workup. Third, the model of care provided at CTCA is a fully integrated team model designed to meet the needs of patients wrth complex diseases and extensive, multi-modality

treatment plans, Incorporation of Naturopathic Doctors into these teams as consultants is possible in states which do not license NDs, but does not allow NDs to function to the full extent of their training. The creation of fully integrated teams for patient populations with less complex disease is not necessarily cost effective or efficient. Finally, in Washington State and Arizona, where CTCA operates facilities in states which do license Naturopathic Doctors, the NDs are highly effective, serving in numerous leadership capacities, and performing tasks which are denied them in states which do not license NDs, including diagnosing, prescribing, and servrngas team leads.

Naturopathic Doctors provide high-quality, professional care to patients seeking solutions to a wide range of health conditiohs. Only a Naturopathic Doctor who is trained in a comprehensive, rigorous, science-based training program has the skills and knowledge to help patients with complex medical conditions make good decisions about the incorporation of natural therapies into their medical care. HB 1717 protects the citizens of the Commonwealth of Pennsylvania by establishingminimum standards for education and training for Naturopathic Doctors.

Thank you for this opportunity to address the committee today. I would be happy to answer any questions that you may have.

References

1. Supportive Care in Cancer. 2005 Nov;13(11):912-9. "The use of dietary supplements in a community hospital comprehensive cancer center: Implications for conventional cancer care." Gupta D, Lis CG, Birdsall TC, Grutsch JF.

Abstract

GOALS OF **WORK:** There is little data on the prevalence of use of dietary supplements in cancer, especially in light of the growing evidence that some dietary supplements can have adverse interactions with conventional cancer treatment. The purpose of this study was to investigate the use of dietary supplements among adult cancer patients in a community hospital comprehensive cancer center.

PATIENTS AND METHODS: A survey of 227 new adult' cancer patients presenting for treatment for the first time at Cancer Treatment Centers of America at Midwestern Regional Medical Center, between November 2001 and October 2003. Patients completed the McCune Questionnaire, a validated instrument that capture?information on the use of 56 dietary supplements in cancer, at admission to the hospital.

RESULTS: Of the 227 patienrs, 73% used some form of dietary supplements during the 30 day period before the survey was conducted. Dietary supplement use was significantly higher ($p = 0.04$) in patients with colorectal (80%) and breast (75%) cancer as compared to patients with lung cancer (53%). Patients with stage II (86%) and III (76%) disease at diagnosis were more likely ($p = 0.02$) to use dietary supplements as compared to those with stage I (71%) disease at diagnosis, while those with stage IV (61%) disease at diagnosis were least likely to use them. Of the 80 patients who had received chemotherapy wirhin the last 30 days, 71% had also used dietary supplements in that timeframe and 25% had consumed one or more herbal therapies that are suspected to have adverse interactions with chemotherapy. Of the 57 patients combining chemotherapy with dietary supplements, 52.6% did not consult a healthcare professional.

CONCLUSIONS: In our study, twenty-five percent of patients receiving chemotherapy were concurrently using dietary supplements suspected to have adverse interactions with chemotherapy, usually relying on information sources other than healthcare professionals. Given the prevalence rates of these agents, healthcare providers should systematically inquire about them, and consider the potential for drug-dietary supplement interactions in treatment planning.

2. Current Drug Metabolism 2007 Feb;8(2):157-71. **"A** mechanistic study on altered pharmacokinetics of irinotecan **by** St. John's **wort."** Hu ZP, Yang XX, Chen X, Cao J, Chan E, Duan W, Huang M, Yu XQ, Wen JY, Zhou SF.

Abstract

Irinotecan (CPT-11) is an important anticancer drug in management of advanced colon cancer. A marked protective effect on CPT-11-induced blood and gastrointestinal toxicity is obtained by combination of St. John's wort (SJW) in recent clinical and rat studies. However, the mechanism is unclear. This study aimed to explore the effects of SJW on the pharmacokinetics of CPT-11 and its major metabolites (SN-38 and SN-38 glucuronide) in rats and the underlying mechanisms using several in vitro models. Short-term (3 days) and long-term (14 days) pretreatment with SJW were conducted in rats to examine the effects of co-administered SJW on the plasma pharmacokihetics of CPT-11, SN-38 and SN-38 giucuronide. Rat liver microsomes and a rat hepatoma cell line, H4-II-E cells, were utilized to study the effects of aqueous and ethanolic extracts (AE and EE) and major active components [hyperforin, hypericin and quercetin) of SJW

on CPT-11 and SN-38 metabolism and intracellular accumulation. Co-administered SJW for consecutive 14 days significantly decreased the initial plasma concentration (C0) of CPT-11, the area under the concentration-time curve (AUC(0-10hr)) and maximum plasma concentration (Cmax) of SN-38. The ethanolic extracts (EE) of SJW at 5 microg/ml significantly decreased SN-38 glucuronidation by 45% ($P < 0.05$) in rat hepatic microsornes. Pre-incubation of aqueous SJW extracts (AE) at 10 microg/ml, SJW EE at 5 microg/ml, and quercetin at 10 microM significantly increased the glucuronidation of SN-38 in H4-II-E cells. A 2-hr pre-incubation of quercetin (100 microM) significantly increased the intracellular accumulation of CPT-11 ($P < 0.05$). However, pre-incubation of hypericin (20 nM and 200 nM) and hyperforin (1 microM) significantly decreased the intracellular accumulation of CPT-11. In addition, pre-incubation of hypericin, SJW EE and quercetin significantly increased the intracellular accumulation of SN-38. Aqueous and ethanolic SJW extracts and its majoractive components did not alter the plasma protein binding of CPT-11 and SN-38. These results indicated that the aqueous and ethanolic extracts of SJW and its major active components could markedly alter glucuronidation of SN-38 and intracellular accumufation of CPT-11 and SN-38, which probably provides partial explanation for the altered plasma pharmacokinetics of CPT-11 and SN-38 and the antagonizing effects on the toxicities of CPT-11. Further studies are needed to explore the role of both pharmacokinetic and pharmacodynamic components in the protective effect of SJW against the toxicities of CPT-11.

3. Cancer Res. 2002 Jul 1;62(13):3868-75. "Dietary **curcumin inhibits** chemotherapy-induced apoptosis in models of human **breast cancer.**" Somasundaram S, Edmund NA, Moore DT, Small GW, Shi YY, Orlowski RZ.

Abstract

Curcumin, the major component of the spice turmeric, is used asa coloring and flavoring additive in many foods and has attracted interest because of its anti-inflammatory and chemopreventive activities. However, this agent also inhibits the generation of reactive oxygen species (ROS) and the c-lun NH(2)-terminal kinase (JNK) pathway, and because many chemotherapeutic drugsgenerate ROS and activate JNK in the course of inducing apoptosis, we considered the possibility that curcumin might antagonize their antitumor efficacy. Studiesin tissue culture revealed that curcumin inhibited camptothecin-, mechlorethamine-, and doxorubicin-induced apoptosis of MCF-7, MDA-MB-231, and BT-474 human breast cancer cells by up to 70%. Inhibition of programmed cell death was time and concentration dependent, but occurred after relatively brief 3-h exposures, or at curcumin concentratronsof 1 microM that have been documented in Phase I chemopreventiin trials. Under these conditions, curcumin exhibited antioxidant propertiesand inhibited both JNK activation and mitochondrial release of cytochrome c in a concentration-dependent manner. Using an in vivo model of human breast cancer, dietary supplementation with curcumin was found to significantly inhibit cyclophosphamide-induced tumor regression. Such dietary supplementation was accompanied by a decrease in the activation of apoptosis by cyclophosphamide, as well as decreased JNK activation. These findings supportthe hypothesis that dietary curcumin can inhibit chemotherapy-induced apoptosis through inhibition of ROS generation and blockade of JNK function, and suggest that additional studies are needed to determine whether breast cancer patients undergoing chemotherapy should avoid curcumin supplementation, and possibly even limit their exposure to curcumin-containing foods.

4. Journal of Clinical Oncology, 2007 ASCO Annual Meeting Proceedings. Vol 25, No 18S (June 20 Supplement), 2007: 15142. **"Effect of** complementary alternative medical **(CAM)** therapy on pain and fatigue in pancreatic cancer patients." Birdsall TC, Levin RD, Alschuler L, Daehler M, Birdsall SM, Martin J, Dounaevskaia L, Lis CG, Braun DP

Abstract

Background: Pain and Fatigue are frequent, difficult to manage, and negatively impact quality of life (QOL) in pancreatic adenocarcinoma patients (PCpts) causing some to seek CAM therapy in place of or in conjunction with conventional analgesics. But the efficacy of CAM on pain and fatigue has not been adequately tested in controlled trials. We employed an alternative strategy by abstracting pain arid fatigue scores from the EORTC-QLQ-C30 questionnaire administered to PCpts treated at Midwestern Regional Medical Center, an integrative oncology center offering conventional and CAM treatment.

Methods: 50 PCpts treared with chemotherapy and/or radiation clinically appropriate for advanced PC ± CAM were evaluated. The CAM group (n=36) had 70%, 11%, and 19% and the nonCAM group (n=14) 71%, 14%, and *25%* Stage IV, III, and II tumors respectively. PCpts received narcotic and anti-inflammatory agents consistent with ASCO and NCCN guidelines. CAM treatments included Green Tea Extract; Melatonin; and high-potency multivitamins Basehne, **3** month(M), and 6M data were analyzed.

Results: Median baseline, 3M and GM pain scores were 50; 0; **33.3** and 75; 16.6; 83 **3** for CAM and nonCAM respectively, not significant (NS) CAM vs nonCAM at any time point by non-parametric tests. Pain control at 3M was improved significantly vs baseline levelsfor each cohort; p=0 02 (CAM) arid 0.03 (nonCAM) by paired 2 tail τ tests. The relative numbers of PCpts with manageable pain (≤ 33) were comparable tor CAM vs nonCAM at baseline (41% vs 36%) and 3 M (81% vs 90%), but not at 6M (67% vs *22%* CAM vs nonCAM respectively, ($p<0.05$ by $?^2$ test). Median baseline, 3M and 6M fatigue scores were: 55.5; 33.3; 33.3 and 44 4; **33** 3; 66.6 for CAM and nonCAM respectively (NS, CAM vs nonCAM at any time point) **By** paired 2-tail t tests, J M (p=0 01) and 6M (p=0 02) values were improved significantly **vs** baseline in CAM but not nonCAM cohorts.

Conclusion: This exploratory study shows that CAM treatment may Improve fatigue and extend the period of effective pain control by conventional analgesics in PCpts. Given the negative impact exerted by pain and fatigue on QOL in this difficult to manage malignancy, CAM Treatment appears to have efficacy for PCpts.