interprted with caution. It will be important to look at apparent calcitriol values by different methods in patients being treated with standard and other dose regimens of calcipotriol.

We felt it important to communicate these observations quickly because many people using this assay may find their results difficult to interpret unless a careful drug history is taken. Of course, these observations will need to be confirmed by further clinical and laboratory studies.

References


S. J. Iqbal* P. Whitaker J. Bourke R. Mumford P. Hutchinson Depts. of Chem. Pathol. and Dermatol. The Royal Infirmary Leicester LE1 5WW, UK

L. W. Le Van Continental Assays Corp. 313 Beltline Highway Madison, WI

* Author for correspondence.

A spokesman for IDS Ltd. comments:

To the Editor:

The structure of calcipotriol is such that it will be detected by assays for 1,25-dihydroxyvitamin D that do not use full HPLC in sample purification, i.e., all currently available commercial kits for 1,25-dihydroxyvitamin D.

It is clear from the information presented by Iqbal et al. that "high doses of topical calcipotriol" may give rise to high concentrations of "apparent" 1,25-dihydroxyvitamin D. However, pertinent information regarding the actual doses used, the site of application (e.g., the highly vascularized scalp?) and the timing of sampling is absent.

In an earlier publication [1], these authors used "high doses" [200–300 g of calcipotriol ointment (50 μg/g), or 2–3× the manufacturer’s maximum recommended dose] and demonstrated changes in serum calcium and intact parathyroid hormone. This might suggest a real need to monitor serum calcipotriol where such high doses are used in the treatment of (e.g.) psoriasis, to avoid unwanted side effects on calcium homeostasis. The authors might wish to consider the IDS 1,25-dihydroxyvitamin D RIA for this purpose if they continue to use such high-dose treatment regimens.

The observations of Iqbal et al. are of potential importance in those situations where laboratory requests for 1,25-dihydroxyvitamin D determinations are received in the absence of information regarding current patient therapy. This is unlikely to result in misdiagnosis, and may be of benefit in situations where excessive use is made of topical calcipotriol treatments.

References


Roger Duggan IDS Ltd. Boldon Business Park, Boldon Tyne & Wear NE35 9PD, UK

More on Antioxidant Activity of Resveratrol in Red Wine

To the Editor:

In light of the letter by Miller and Rice-Evans [1], I have reread my original editorial [2] no fewer than one dozen times. Nonetheless, I cannot find therein the notion that resveratrol is the major component responsible for the antioxidant activity of red wine. In fact, I specifically acknowledged that resveratrol is "not as effective as certain other wine flavonoids" in preventing low-density lipoprotein oxidation, and cited the paper by Frankel et al. [3] to prove my point. Before even getting to the stage of mentioning its antioxidant potential, I described its other properties, including inhibition of hepatic lipid synthesis [4], which, incidentally, we have now confirmed by using the human liver cell-line, Hep G2 [5,6]; its inhibition of eicosanoid synthesis and platelet aggregation [7,8], which we have recently demonstrated for human platelets [9] and leukocytes [4]; and its inhibition of protein tyrosine kinase activity [10]. Although its antioxidant potential is many times greater than that of vitamin E on a molar basis, in the context of my review this was the last and also the least of its many attributes.

Not being versed in the sciences of enology and viticulture, Miller and Rice-Evans may be excused the lack of perspective in taking the data of Frankel et al. [11] at face value and lavishing upon them the meticulous mathematics that resulted in their Table 1. A host of publications from our laboratory [12,13] and others [14,15] have reported concentrations of resveratrol and related polyphenols in wines from other regions and countries many-fold higher than those of Californian wines. In addition, I drew attention to the existence in wine of various isomers and glucosides (to which should be added polymers) of resveratrol other than trans-resveratrol, the only form assayed by Frankel et al. [11], which also are likely to be effective and bioavailable.

The unique aspect of resveratrol, apart from its apparent ability (at least in vitro) to favorably modulate many biological processes that lead to atherosclerosis and coronary heart disease (CHD), is that, unlike the other polyphenols mentioned by Miller and Rice-Evans, it is not a constituent of the normal human diet. Peanuts and red wine are the only sources identified up to the present. No one has, so far as I am aware, recommended peanuts as an antidote to CHD, but an expanding body of knowledge, partly reviewed in my editorial [2], supports the idea that red wine may be the most efficacious alcoholic beverage offering protection against this disease. If that is so, then its polyphenolic content is probably what makes the difference. Frankel et al. [11] have calculated that two glasses of red wine per day would add an additional 40% of antioxidant nutrients to the average North American diet. But is there any evidence that the latter is deficient in antioxidants? Unless it is, then the beneficial effects of red wine are likely to be due to its alcohol content alone, unless some other bioactive constituent is present in this delectable fluid and not in other components of the diet. Resveratrol fulfills these criteria. Is it the "magic bullet" concealed in the scarlet liquid which, by tradition, should accompany red meats, game, and strong cheeses? At present, we don't
know, my colleagues and I intend to find the answer.

References

14. Jeanet P, Bessis R, Maumèse BF, Stoghi M.

Table 1. Patients with Increased cTnI.*

<table>
<thead>
<tr>
<th>No.</th>
<th>Age, years</th>
<th>Sex</th>
<th>cTnI, µ/L</th>
<th>cTnT, µ/L</th>
<th>LD1/LD2</th>
<th>CK, µ/L</th>
<th>CK-MB, µ/L</th>
<th>Cr, mg/L</th>
<th>Diagnosis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67</td>
<td>M</td>
<td>1.2</td>
<td>0.79</td>
<td>0.92</td>
<td>156</td>
<td>3</td>
<td>132</td>
<td>DM; HTN</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>F</td>
<td>1.3</td>
<td>0.23</td>
<td>0.67</td>
<td>116</td>
<td>1</td>
<td>27</td>
<td>DM; HTN</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
<td>M</td>
<td>1.4</td>
<td>0.15</td>
<td>0.67</td>
<td>100</td>
<td>1</td>
<td>36</td>
<td>DM; hepatitis C</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>M</td>
<td>1.5</td>
<td>0.18</td>
<td>0.51</td>
<td>687</td>
<td>8</td>
<td>39</td>
<td>Hepatic failure</td>
</tr>
<tr>
<td>5</td>
<td>77</td>
<td>M</td>
<td>3.6</td>
<td>4.25</td>
<td>0.81</td>
<td>60</td>
<td>3</td>
<td>62</td>
<td>Non-Q-wave MI; CHF</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>M</td>
<td>2.8</td>
<td>0.25</td>
<td>0.59</td>
<td>480</td>
<td>11</td>
<td>38</td>
<td>Non-Q-wave MI; hepatic injury</td>
</tr>
<tr>
<td>7</td>
<td>87</td>
<td>M</td>
<td>1.6</td>
<td>1.30</td>
<td>0.59</td>
<td>354</td>
<td>2</td>
<td>34</td>
<td>HTN; urosepsis; gout</td>
</tr>
</tbody>
</table>

* Reference values: cTnI <0.35 µg/L; cTnT <0.1 µg/L; lactate dehydrogenase isoenzyme 1 and 2 ratio (LD1/LD2) 0.6; creatine kinase (CK) 50–150 U/L (male), 40–120 U/L (female); CK-MB isoenzyme 0–4 µg/L; serum creatinine (Cr) <14 mg/L.

* DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction; CHF, chronic heart failure.

Greater Frequency of Increased Cardiac Troponin T than Increased Cardiac Troponin I in Patients with Chronic Renal Failure

To the Editor:

In a previous report we documented that cardiac troponin T (cTnT) was increased in 52 of 82 (63.4%) patients with end-stage renal disease (ESRD) without clear evidence of myocardial injury as defined by usual criteria, i.e., history of chest pain, compatible electrocardiographic abnormalities, and (or) concurrent increased concentrations of CK-MB or "flipped" lactate dehydrogenase isoenzymes LD1/LD2 ratio at the time of testing [1]. We were unable in that study to determine whether the increased cTnT in renal failure was due to assay cross-reactivity from skeletal muscle cTnT, reexpression of cTnT during muscle regeneration, or subclinical myocardial injury. With the availability of the more organ-specific cardiac troponin I (cTnI) assay [2], we have been able to measure cTnI concentrations in 79 of 82 patients, using the original specimens subsequently frozen and preserved from the previous study. We used the Stratus® system (Dade International, Miami, FL) for cTnI, following the instructions of the manufacturer. The reference range in

this study for cTnI is ≤0.35 µg/L; for cTnT, <0.1 µg/L. The discriminator value for cTnI is >1.5 µg/L; for cTnT, >0.2 µg/L. Interassay imprecision (CV) for cTnI in our laboratory is ≤10%.

Of the 79 patients with ESRD, 7 (8.9%) had measurable cTnI, with values ranging from 1.2 to 3.6 µg/L. All the other patients had undetectable cTnI, i.e., below the limit of detection of 0.35 µg/L. Salient characteristics of this subset are shown in Table 1. All of these patients had concordant increases in cTnT concentrations. In three of these ESRD patients, the cause of chronic renal failure was diabetic nephropathy. It is interesting that three additional patients also had concurrent hepatitis (drug-induced in two, hepatitis C in one) with marked increases of transaminase concentrations. Reported clinical trial data on 128 patients who had been ruled-in for acute myocardial infarction indicated that the discrimination value for cTnI was 1.5 µg/L (unpublished data, Dade International). If we use this cutoff value, none of the patients with diabetic nephropathy had diagnostic cTnI values consistent with an occult or silent infarction, although minor myocardial injury appears likely.

To determine whether the other four patients who had increases in both cTnT and cTnI experienced subclinical myocardial injury, we scrutinized the clinical findings and laboratory data. The two patients with the highest values for cTnI (3.6 and 2.8 µg/L) did have subsequent clinically confirmed non-Q-wave infarction, which was recognized during the latter part of their hospitalization. We attribute the earlier result detected in these two patients as representing subclinical infarction with later extension resulting in clinical recognition [3]. In