Modelling the Consequences of Variability in Food Production Chains on Human Health

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Keywords: epidemiology, Monte Carlo simulations, bioactive compounds, processing, glucosinolates, vegetables, Brassica

Abstract

Epidemiological studies on the relation between fruit and vegetable intake and chronic diseases show variable results. In many studies a small protective effect is found for fruit and vegetable intake and the risk for cardiovascular diseases and cancers. In other studies these effects could not be found in a statistically significant way. Experimental animal and mechanistic studies with cell lines or in humans show often clear protective effects of many phytochemicals like e.g. glucosinolates, flavonoids and carotenoids. In this paper the effect of variability in the food production chain on the results of epidemiological studies as predicted by probabilistic simulation studies is presented. Even if a very strong protective effect of a phytochemical is assumed, this variability will lead to only very small, non-significant, protective effects to be found in epidemiological studies. The effect of different scenarios to improve human health has been investigated. Increasing the fruit and vegetable consumption will produce far less benefits when compared with a scenario of increasing the level of phytochemicals and reducing the variability in its content.

INTRODUCTION

During the last decades there is a considerable interest in the relation between our diets and our health. Of major interest is the relation with chronic diseases like cardiovascular diseases and different forms of cancer. Different types of studies have addressed this issue: epidemiological, animal and mechanistic studies. The most direct type of study in relation with humans seems to be epidemiological cohort studies with the occurrence of the actual disease as endpoint. In these types of studies many associations have been found between fruit and vegetable intake and the occurrence of chronic diseases (e.g. Steinmetz and Potter, 1996). The observed associations are mostly protective effects of a high intake of fruit and vegetables. The observed effects are, however, small and not always significant. A large recent study showed no significant effect of high fruit and vegetable intake on cancer and a small significant effect on cardiovascular diseases (Hung et al., 2004).

Mechanistic studies and experimental animal studies focus on the effect of individual components from our foods. The majority of the studies focus on the effects of phytochemicals like: flavonoids, other polyphenols, carotenoids, glucosinolates, different fibres and so on. Many protective mechanisms of the various components have been identified. Also many studies have been reported on effects of the intake of specific compounds on biomarkers in the human body for protective effects.

From these two lines of research one could raise the question why the protective effects found in mechanistic studies are not found in a stong significant way in epidemiological cohort studies. Are the protective effects in real life just not there, or is there another reason responsible for this. As published before the variability in the content of phytochemicals in plant foods can be enormous (Dekker et al., 2000, Dekker and Verkerk, 2003). This variability may well be responsible for a large amount of scatter in results from epidemiological studies that are only measuring the intake levels of products, and not the actual intake of the protective components (Dekker and Verkerk, 2005). In

this paper the effects of various steps in the production chain on the level of glucosinolates will be presented. This information is used as a case study to determine the consequences of this variation on the results of epidemiological studies. The effect of the shape of the component intake versus risk reduction on the statistical power of epidemiology is investigated. In addition some possible scenarios are simulated for improving public health either by increasing fruit and vegetable intake or by increasing the content and lowering its variability.

MATERIALS AND METHODS

Monte Carlo simulations were done with Decision Tools software (Palisade).

The conceptual scheme for using Monte Carlo simulations to predict the effects of the variability in food production chains on the outcome of epidemiological studies is shown in Figure 1. For each simulation 30,000 consumers were simulated. More details on the simulation procedure are described in previous research (Dekker and Verkerk, 2003).

For the quantitative description of the variability in phytochemicals, the data on glucosinolate levels as determined in various stages of the food production chain were used (Verkerk, 2002; Tebbenhoff, 2003).

RESULTS AND DISCUSSION

Variability

The variation of glucosinolate levels throughout the chain has been determined in a quantitative way. Effects of cultivar, storage, industrial (thermal) processing and domestic cooking have been studied. As an example the variation in the level of two glucosinolates in 170 samples from 12 varieties of Brassica vegetables is shown in Figure 2.

As can be seen from Figure 2, the variation in the different samples from different cultivars is well over 100-fold. This variation could be described by a log-normal distribution using the “BestFit” procedure in the Decision Tools software, that evaluates the fit results for different kinds of distribution to the actual data. Even if only Broccoli samples are taken into account the variation is well over 20-fold. In addition to this variation also further processing will add to the final variability. In a previous paper (Dekker and Verkerk, 2003) this variation was also described by log-normal distributions. For simplicity, here we will use overall distribution taken into account the cultivar variation as well as the processing/preparation variation. The estimated distribution in the level of phytochemical is a log-normal distribution, with a mean value of 10^{-3} AU, a standard deviation of $3 \cdot 10^{-3}$, which was truncated at a maximum of $5 \cdot 10^{-2}$ AU. Arbitrary units were used since although the data from glucosinolates were used, the calculations of the further consequences of variability are not limited to this particular group of compounds.

Simulation of Epidemiology

For the calculation of the actual intake of products containing the health promoting compound the calculation scheme as depicted in Figure 1 is used. For product consumtion data three intake groups were defined as depicted in Figure 3.

In the Monte Carlo simulations a sample from the product intake was multiplied with a sample from the distribution on the level of the phytochemical. This resulted in a calculated phytochemical intake.

The next step is to link this intake figure with a reduction in risk for a chronic disease like cancer. The exact relation between these two variables is unknown however. The aim of this simulation is to predict the measured health effect with the assumption that there is a (strong) protective effect of the phytochemical. Therefore three different protective relations were investigated as shown in Figure 4.

These risk reduction curves were described by the equations 1-3, assuming there will always be a remaining relative risk of 20% not influenced by phytochemical intake.

$$RR = 0.2 + 0.8 \cdot e^{-5 \cdot C} \quad (1)$$

$$RR = 0.2 + 0.8 \cdot \frac{1 + 20 \cdot e^{-10 \cdot C}}{1 + 20 \cdot e^{-10 \cdot C}} \quad (2)$$

$$RR = 0.2 + 0.8 \cdot \frac{1 + 100 \cdot e^{-10 \cdot C}}{1 + 100 \cdot e^{-10 \cdot C}} \quad (3)$$

The obtained relative risk is subsequently translated into an absolute risk by multiplying with 0.01 (this value is estimated from the reported cases of colon/rectal cancer in a recent cohort study from Voorrips et al, 2000). In order to simulate whether an individual will develop cancer this calculated absolute risk was compared with a 'fate of life' factor that was randomly picked from a uniform distribution between 0 and 1. If this 'fate of life' factor was lower than the absolute risk value the consumer was marked as a cancer patient in the study.

In reality some of the variation caused by cultivar differences will level out because of the multiple consumption moments over the years that these studies take. The type of products and the way of domestic cooking, however, can be expected to be not so variable for each individual and therefore the variation caused by these steps will not level out. Because of the fact that only three sources of variation within the food production chain were taken into account, while the complete chain will consist of at least 6 steps with each multiple sources of variation, the real variation might in fact be underestimated by the approach taken here.

For the three protective effect relations (equations 1-3) the outcome of an epidemiological study is shown in Figure 5.

From Figure 5 it can be seen that only for the protective effect relation nr. 3 the reduction in relative risk calculated from the epidemiological study is significantly lower for the high intake group compared to the low intake group ($p<0.05$). In a previous publication (Dekker and Verkerk, 2003) the effect of the strength of the protective effect on the statistical power of the epidemiological study was investigated. Here we can also conclude that besides this strength also the shape of the curve of risk vs. phytochemical intake will determine wheter a health effect will be picked up by epidemiological studies.

From these results one can conlude that, due to the enormous variability in content of bioactive components in vegetables, epidemiological studies based on only the product intake data will only pick up protective effects of certain product groups if the effect of the components present in that product group have a very large protective effect. It seems therefore tempting to conclude that when a significant effect is indeed observed in epidemiological studies, the actual effect of the responsible compound(s) in the protective products should have been really strong.

Scenario Modelling

An interesting application of these simulations is to predict the effect of possible scenarios to improve human health. The effect of increasing fruit and vegetable consumption by 50% and the effect of increasing the concentration 3-fold while lowering its variability 3-fold of the protective phytochemical in the fruit and vegetables were calculated. The result on the prediction of the total number of cancer cases is presented in Table 1.

From Table 1 it is clear that increasing the content and reducing the variation is far more effective in increasing human health. Also the health effects are more consistently measured in that case. Of course the predictions presented here rely fully on the assumed protective effect relations, which in fact cannot be derived from studies on the health effects of phytochemicals at present.

CONCLUSIONS

Many steps in the food production chain of fruit and vegetable products can have a large impact on the final human intake of health protective components. In epidemiological studies this variation in the content of phytochemicals in similar products is usually not taken into account. This makes epidemiological cohort studies a very insensitive tool to pick up health promoting compounds. If an effect is observed, the effect of reducing the variation is expected to have an enormous impact on health promotion. Although still a lot of uncertainty exists in the scientific community as to the questions what are the effective phytochemicals and what is the mechanism of protection, a probabilistic simulation approach as presented here is a valuable one to evaluate different scenarios for effectively using phytochemicals in our diets to improve human health.

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Tables

Table 1. Predicted number of cancer cases in a cohort of 30,000 people.

Scenario:	Predicted cases	Significance ($p<0.05$) of RR difference between L and H intake group
Reference situation	220	Only for relation 3
Product intake +50%	200	Only for relation 3
Content up 3-fold, SD down 3-fold	120	Yes (all relations)

Figures

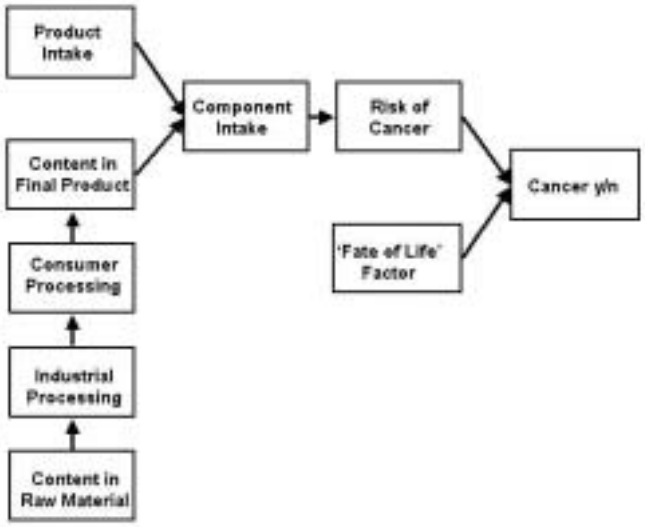

Fig. 1. Schematic scheme for the Monte Carlo simulations (Dekker and Verkerk, 2003).

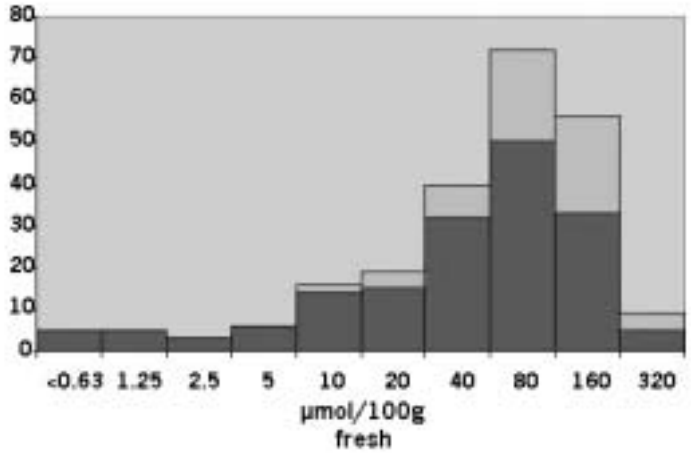

Fig. 2. Distribution in the level of glucoraphanin plus glucoiberin in 170 samples from 12 varieties of Brassica vegetables (area in light grey is the distribution for Broccoli only, data taken from Tebbenhoff, 2003).

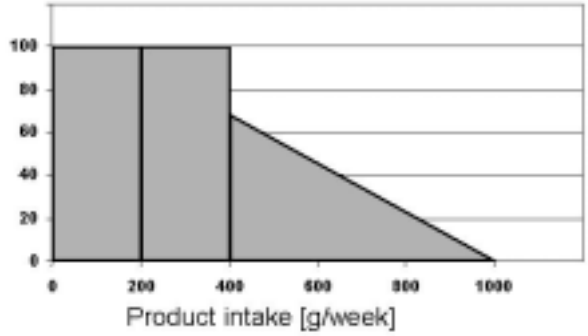

Fig. 3. Product intake groups with low (0-200), medium (200-400) and high intake (400-1000).

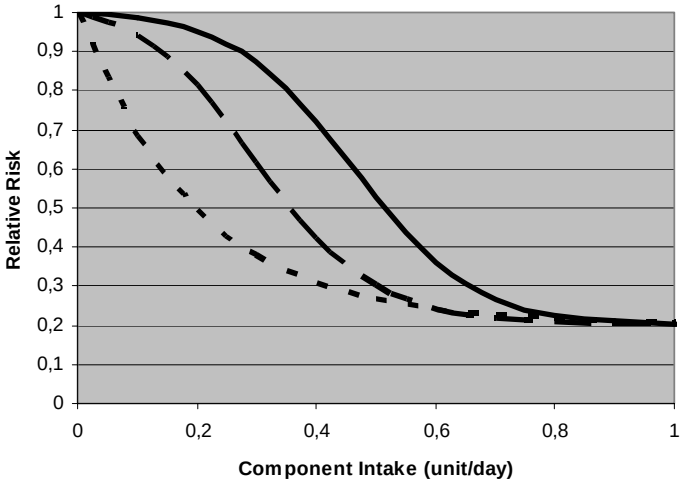

Fig. 4. Assumed effects on relative risk of cancer of intake of protective component (lines from left to right correspond to different relations as described in the text by equation 1,2 and 3 respectively).

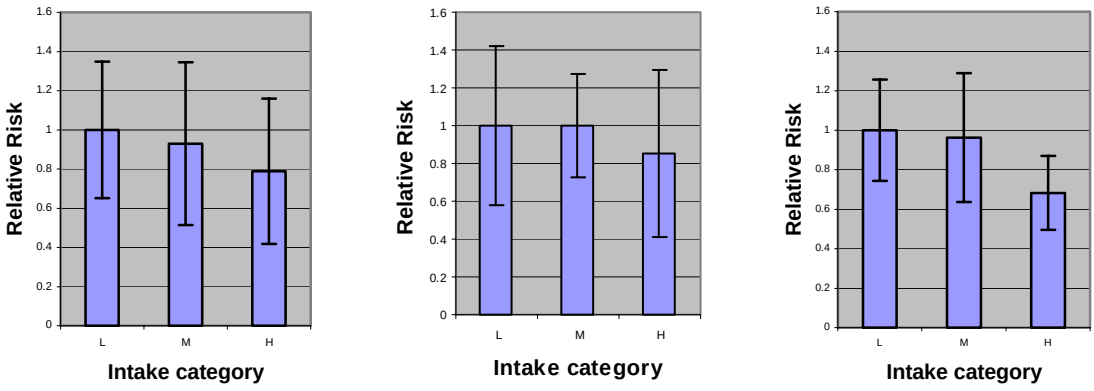

Fig. 5. Results of the simulation of the epidemiological cohort study according to the three protective effect relations (From left to right: equations 1, 2 and 3 respectively, L=Low intake, M=Medium intake, H=High intake group).