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Resveratrol Antioxidants and Cancer: A Review of The Efficacy and Mechanism of Resveratrol on The Metabolism of Varying Types of Cancer Cell Lines

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Resveratrol is a naturally occurring substance found in foods such as fruits. In addition to having antioxidant properties [1], they are purported to have inhibitory effects on the metabolism of certain cancer cells. Three different studies that were conducted within the last 12 years are examined, and each of these studies research the effects that resveratrol has on cancer cells. The first study, published in 2000, explores how resveratrol inhibits the growth of colonic cancer cells [1]. The second study, which was published in 2002, observes the effect that resveratrol has on several distinct types of cancer cell lines and how resveratrol concentration affects the growth rate of those types of cancer cells [3]. The final study occurred in 2007 and conducted in-depth research on how resveratrol induces autophagy in ovarian cancer cells and how it may be related to glucose metabolism in those cancer cells [2]. Lastly, the results of each study are examined to see how they further the current knowledge base of resveratrol and cancer cells, and see which questions that the results of the studies do not answer.

Introduction

Cancer is a disease that occurs when certain cells within the human body grow rampantly and uncontrollably due to an abnormality or defect in those cells' function. It is thought that normal cells become cancer cells through genetic damage, which can cause the cell to lose control of its cell division and cell growth regulation systems [4]. The exact effect that cancer can have on an afflicted person can vary, depending on the organ system affected by the cancer. The effect of the cancer can also vary depending on the cancer's ability to metastasize (its ability to spread to other organ systems). Thus, cancer can cause a sharp decline in an afflicted person's health or even result in the death of said person. Cancer is also a prevalent disease within the United States, with 1,638,910 new cancer cases expected to occur in 2012, and 577,190 of those cases are expected to result in the death of the patient [4].

Due to the increasing cost of cancer and the increasing number of annual cancer cases in the United States [4], there has been great interest in discovering new methods of treating or preventing cancer that are cost-effective and have minimal side-effects on those individuals who undergo cancer treatment or cancer prevention regimens. Recently, there has been research conducted on a substance known "Resveratrol", a naturally occurring polyphenol that is found in certain plants and in certain food products such as grapes and red wine [1], and how it affects the metabolism of cancer cells. The purpose of this review is to explore how resveratrol interacts with the metabolic processes of several different types of cancer cells in several original research studies. It is also used to gauge the efficacy of resveratrol as a cancer treatment agent for those same types of cancer cells. The various studies on resveratrol that are covered in this review will also be critiqued.

Recent Progress

In the last 12 years, there have been several studies conducted on the effects of resveratrol on several distinct types of cancer cells. Of the studies reviewed in this paper, three such studies were conducted on cancer cells grown in cultures. Each of these studies were intended to observe the ways in which resveratrol interacted with cancer cells to act as an anti-cancer agent.

The first study, published in 2000, experimented on a particular cell line of colonic cancer cells known as CaCo-2 [1]. These cells were grown in separate cultures, and exposed to differing concentrations of resveratrol, which were introduced to the media after the cell cultures after 24 hours worth of growth [1]. It was observed that the CaCo-2 cell cultures' growth was inhibited by resveratrol, with higher concentrations of resveratrol resulting in more inhibition of cancer cell growth; it is important to note, however, that cancer cell growth was not halted by the resveratrol, only slowed [1]. It was discussed that might imply that the effects of resveratrol are reversible or can otherwise be mitigated. It was also observed that resveratrol treatment significantly decreased the activity of the enzyme "ODC", or Ornithine Decarboxylase, [1] which is necessary for cell division and growth.

The second study was published in 2002, and observed the effects of resveratrol on several different types of cancer cell lines: Seg-1 and Bic-1 (esophageal cancer cells), SW480 (colon cancer cells), MCF7 (breast cancer cells), HCE7 (also esophageal cancer cells), and HL60 (leukemia cells) [3]. Each of these cell lines were grown in cultures, and exposed to differing concentrations of resveratrol, and were measured for levels of apoptosis, protein expression, and cell distribution [3]. The results of this study showed that resveratrol causes inhibition of growth in cancer cell lines proportional to the concentration of resveratrol given, and that resveratrol can induce apoptosis in certain types of cancer cells [3]. Further analysis showed that the growth-inhibiting effect of resveratrol stems from its ability to interfere with cancer cells' ability to synthesize DNA [3]. However, resveratrol was not equally effective on all of the cancer cell lines. In particular, the Bic-1 cancer cell line seemed to be resistant to resveratrol's effects, and did not suffer from as much growth inhibition as the other cancer cells. It was also observed that Bic-1 and MCF7 cancer cells underwent significantly less apoptosis due to resveratrol than the other cancer cell lines [3]. The apoptotic effects of resveratrol on the cancer cell lines were summarized in Figure 1.

The most recent research covered by this review article occurred in 2007. Previous research conducted by these researchers showed that resveratrol induced autophagy in human ovarian cancer cells [2] (autophagy occurs when the cell dies due to lysozome activity, distinct from apoptosis). When the researchers observed that ovarian cancer cells will undergo autophagy when deprived of glucose, it was theorized that reveratrol may induce a similar deprived state in the ovarian cancer cells that it effects [2]. Thus, this particular study was conducted to investigate the pathways involved in resveratrol-induced autophagy in these types of cancer cells. Cancer cell lines were grown on several types of media: one media contained no glucose, another contained added resveratrol, another lacked amino acids, and the final media had no nutrients added or removed from it [2]. It was observed that ovarian cancer cell cultures that were grown in glucose-deprived media underwent autophagy at similar rates as ovarian cancer cells that were grown in media with added resveratrol. The results of the study also showed that there was decreased expression of the signaling molecules "pAKT", "tAKT", "pmTOR", and "tmTOR" in cancer cells that grew in media with added resveratrol [2]. It is important to note that all these signaling molecules play a role in regulating cellular carbohydrate metabolism and cellular glucose uptake.

Discussion

The results of the reviewed studies appear to indicate that resveratrol does have some anti-cancer properties. It can inhibit enzyme activity in certain types of colon cancer [1], induce apoptosis in cancer cells [3], and can inhibit the expression of molecules that regulate a cancer cell's glucose uptake and metabolism [2]. All of these things play an important role in cancer metabolism, and all relate directly to cancer cell growth. Resveratrol does not affect all types of cancer cells equally, however. The Bic-1esophageal cancer cell line and MCF7 breast cancer cell line showed a degree of resistance to resveratrol's effects, and were not as greatly inhibited as other types of cancer [3]. These studies do not appear to examine if there is any uniform reaction that cancer cells have when exposed to resveratrol, either. This may imply that cancer is not a disease of uniform composition, and that the metabolic processes of one type of cancer cell can differ greatly from those of other types of cancer cells.

Another point to consider is the fact that all of these studies were conducted on cancer cells that were grown in cultures [1] [3] [2]. The effects of resveratrol in these studies can only tell of what happens to cancer cells if resveratrol is directly applied to those cancer cell cultures. As such, these results may not be indicative as to the efficacy of resveratrol as an anti-cancer agent if applied to cancer cells in another manner. Thus, the results of the reviewed studies do not address the problem of how resveratrol can be effectively applied to a situation that does not involve a cancer cell line culture. To do such a thing, it may be necessary to conduct studies on animal test populations or even perform case studies on human volunteers.

Overall, the results of these reviewed studies show that resveratrol can have an inhibiting effect on the metabolism of certain types of cancer cells. As it stands, additional studies must be conducted to gauge its effectiveness as a part of a cancer treatment or cancer prevention regimen. But with the abundance of resveratrol in food sources such as grapes [1], it may present a

readily available source of anti-cancer agents that lack the side effects of current cancer treatment options such as chemotherapy.

References

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Figures

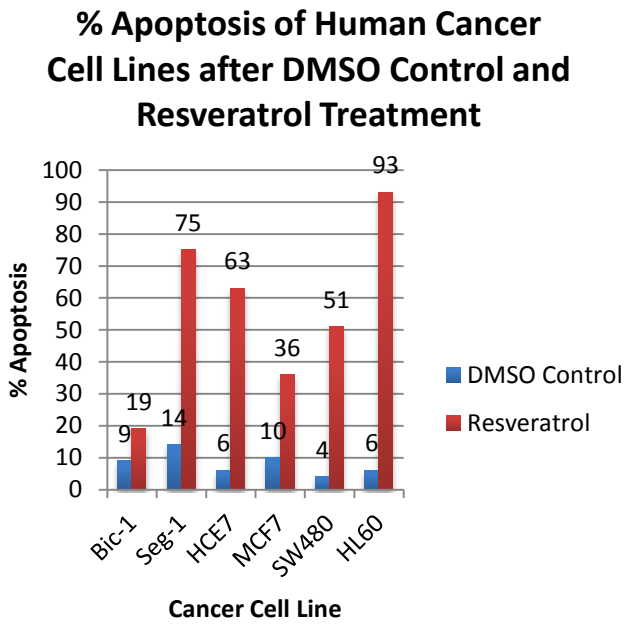

Figure 1

