CHAPTER 37

Benzaldehyde in cancer – oxidant and strong structurer of cytoplasmic water with effect on several neoplasias

Acute myelocytic leukemia, malignant lymphoma, multiple myeloma, leiomyosarcoma, and carcinomas of the tongue, parotid, lung, breast, esophagus, stomach, liver, pancreas, colon, rectum, kidneys, brain, bladder and testicular seminoma.

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Orphan drugs also have their place in medicine and must be used. **JFJ**

The attempt to change the structure of the potent anticancer benzaldehyde to patent it resulted in failure. **JFJ**

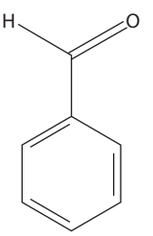
Benzaldehyde is a chemical compound consisting of a benzene ring with an aldehyde radical. It is the simplest representative of aromatic aldehydes and is found in nature in many foods. It gives the coffee and chocolate a special aroma. It has an odor similar to that of almonds being the primary component of the oily extract of bitter almonds. In its simple form is extracted from the apricot, cherries and leaves of the laurel (Laurus nobilis), in its form combined with a glycoside is found in peach seeds, and is called amygdalin.

Amygdalin was used in the treatment of cancer for more than 40 years, known as nitriloside, mandelonitrile, laetrile and vitamin B17. It is present in the core of the seed of apricot, peach, cherry and plum (Song-2014). Amygdalin is converted into the body in benzaldehyde, glucose and hydrogen cyanide (HCN).

It was thought that because the neoplastic cell does not possess rodanase, cyanide metabolizing enzyme, it would be exterminated by this metabolic poison. **Wrong,** they die without inflammation due to benzaldehyde.

We found several reports of cyanide poisoning in the medical literature with the use of amygdalin in cancer. In clinic, we do not use amygdalin; we prefer the safety and absence of side effects of benzaldehyde.

Synonyms: benzoic aldehyde, almond artificial essential oil, benzenocarbon, benzene carboxaldehyde, artificial almond oil, bitter almond oil. Formula: C6H-15CHO and molecular weight: 106.1 g/mol.



Benzaldehyde

Benzaldehyde structures cytoplasmic water: osmotic cosmotrope and oxidant.

The dynamic and constant balance between structured and unstructured water characterizes health. This balance is maintained by factors dependent on the intracellular environment and the interstitial environment.

Benzaldehyde is a frankly hydrophobic inorganic solute. Because it is hydrophobic and relatively low in molecular weight, it is believed that it has the physico-chemical ability to structure the water molecules. On the other hand, benzaldehyde is a potent oxidant

and thus a strong electron acceptor that slows or even prevents the Embeden-Meyerhof cycle. This cycle generates large amounts of pyruvate, a strong destructor of cytoplasmic water. Benzaldehyde preventing the cycle will make it difficult to disassemble.

Thus the action mechanism of benzaldehyde is by direct effect as physical-chemical structurer and indirect effect as electron acceptor, oxidant.

Benzaldehyde as a strong structurant of cytoplasmic and oxidant water causes beneficial effects and even the cure of several types of cancer: acute myelocytic leukemia, malignant lymphoma, multiple myeloma, leiomyosarcoma and carcinomas of the tongue, parotid, lung, breast, esophagus, stomach, liver , Pancreas, colon, rectum, kidneys, brain, bladder and testicular seminoma.

Historic

Studies began with Takeuchi who employed a volatile fraction extracted from the fig, in the Ehrlich carcinoma of mice.

Between 1965 and 1975, 83 patients were treated intravenously with the volatile fraction of the fig. This fraction, difficult to standardize, was effective in 12 patients, 4 of whom responded completely, whereas no response was observed in the remaining 71 patients. By studying the carcinostatic component of the volatile fraction of fig, it was identified that the effective agent was benzaldehyde.

Most importante study

In 1980, Mutsuyuki Kochi et al. published the most important work in the medical literature on the antitumor activity of benzaldehyde in humans, a low-cost and non-toxic drug.

Ninety patients with end-stage inoperable carcinoma and 12 patients in severe clinical conditions with sarcomas received orally or rectally benzaldehyde in the form of beta-cyclodextrin-benzaldehyde (CDBA) at the dose of 10mg/kg/day of benzaldehyde divided In 4 doses. Only the 57 patients who took benzaldehyde regularly for a longer period 1 month were considered.

Medication

Because benzaldehyde is very poorly soluble in water, it is not suitable for intravenous, intramuscular or subcutaneous injection. In this way, a beta-cyclodextrin-benzaldehyde admission administered in the form of capsules or suppositories was prepared. The amount of benzaldehyde in the CDBA is 8.3%, and thus 6g of CDBA contains about 500mg of benzaldehyde.

Outcome of the study

All 57 patients who entered the study had histological confirmation of the tumor diagnosis. Patients had undergone all types of conventional treatment such as surgery, chemotherapy and/or radiotherapy, without therapeutic success and progression of neoplastic disease.

Of the 57 patients, 32 were men, 15 were women and all were in stage of neoplastic disease, being considered terminal patients. The age ranged from 4 to 82 years, with a mean of 53 years. The types of cancer were the most varied: acute myelocytic leukemia (2), malignant lymphoma (2), myeloma multiple (1), leiomyosarcoma (1) and the following carcinomas: tongue (4), parotid (2), lung (9), breast (2), esophagus (2), stomach (10), liver (6), pancreas (4), colon (1), rectum (3), kidneys (2), brain (3), bladder (2), and testicular seminoma (1).

In this study, the administration of benzaldehyde lasted on average 2 years and 5 months and all patients were observed for 4 weeks to more than 2 years.

According to Kochi, of the 57 patients with terminal cancer, 19/57 or 33% presented complete tumor remission; 10/57 or 17.5% presented partial remission (above 50% of regression); 19/57 or 33% were getting better at writing the paper; 7/57 or 12.3% remained with the disease stable and in 2 patients there was progression of the disease.

Of the 9 lung carcinomas, 3 presented complete remission, 3 partial remissions, 1 stabilized and 2 presented disease progression.

Three of the 4 patients with squamous cell carcinoma of the tongue had previously received radiotherapy and chemotherapy and all were in poor clinical condition at the start of treatment. After 1.5 to 6 months of CDBA, all patients with tongue cancer achieved complete remission. In these 4 patients, the most relevant fact was the differentiation for normal and keratinized epidermoid cells. Amazing.

An 83-year-old woman with adenocarcinoma of the rectum and almost complete obstruction of the anal canal completely responded to the CDBA, and surgery was not necessary because the stool now passed freely through the anal canal. Differentiation of adenocarcinoma in normal cells has also been observed here.

A 4-year-old boy with acute myelocytic leukemia had received adriamycin, arabinoside, cytosine, vincristine, prednisolone and methotrexate for maintenance in the last 10 months, however, without achieving remission of the leukemia. Ten days after starting treatment with CDBA, he had complete remission of the leukemia and, in the course of evolution, platelets, leukocytes, and hemoglobin returned to normal levels. Complete remission lasted more than 4 months and there were no toxic effects during treatment.

Despite the persistent oral administration of CDBA, approximately 500mg/day of benzaldehyde for more than 1 year, no toxic effects or hepatic or renal side reactions were observed, leucopenia, thrombocytopenia, anemia, anorexia, vomiting or hair loss were not observed. The therapeutic response lasted while the patient ingested the drug. This fact we understand very well: the author did not remove the causal factors.

Several types of tumor have different sensitivities to benzaldehyde, so in the leiomyosarcoma, doses of 30mg/day have been very effective, already in squamous cell carcinoma or adenocarcinoma doses of 300 to 500mg/day are necessary.

These data were transcribed literally from the work of Kochi, that is, we should not accept these results as definitive because they are very good and patients very serious. It is to want much of only one drug. We did not find repetitions of similar work in the medical literature.

Following is the casuistic of Dr. Kochi taken from his original paper. They are fifty-seven patients who did not respond to the conventional treatment and thus the attempt was made to use benzaldehyde. He observed a large number of total eradication of tumors, a stable disease or an improvement in the quality of life.

Patent Attempts

In 1985, Kochi used a benzaldehyde derivative, 4,6-benzylidene-alpha-D-glucose (BG), in 65 patients with advanced inoperable carcinoma of various types. The dose was 720-1800mg/m2 daily intravenously. There was response in 55% of the patients: 7 achieved complete response; 29 achieved partial response; 24 remained stable and 5 showed disease progression. There were no side effects and increased survival was evident.

In 1990, Tatsumura used intravenous BG in 24 patients: 11 cases of primary lung tumor, 4 cases of metastatic lung cancer, 5 cases of gastric cancer and 1 case of each of the following cancers: colon, liver, pancreas And prostate. There was a beneficial response in 10/24 patients or in 41.7% of the cases. Two complete remissions were observed: pulmonary metastasis of breast cancer and gastric cancer liver metastasis.

Quadro 37.1 Fifty-seven refractory cancer patients treated with benzaldehyde. Retrieved from the original paper of Kochi-1980.

	Nº of patients	Complete	Partial	Improvement	Stable disease	Progression
Carcinoma						
Tongue	4	4				
Parasinus	1		1			
Parotid	1	1				
Lung	9	3	3		1	2
Breast	2	1		1	1	
Esophagus	2		1	0		
Stomach	10	2		8		
Liver	6		2	3	1	
Pancreas	4	1		2	1	
Colon	1	1				
Rectum	3	1		2		
Testis (seminoma)	1				1	
Kidney (Grawiz's tumor)				2		
Brain	3	1			2	
Gall bladder	1	1				
Transitional cell	1		1			
Acute myelocytic leukemia	2	2				
Malignant lymphoma	2		1	1		
Multiple myeloma	1	1				
Leiomyosarcoma	1		1			
Total	57	19	10	19	7	2

Mechanism of action

In his magnificent book entitled "The Living State," Albert Szent-Gyorgyi, the discoverer of vitamin C, claims that all electron-accepting chemicals have the ability to abolish neoplastic cell proliferation, and benzaldehyde is an excellent electron acceptor. Electron or hydrogen ion acceptors are oxidizing agents that increase electronic desaturation. Well, for this Nobel Prize in Chemistry, the level of electronic desaturation dominates evolution – it dominates life.

Normal cells are in the "beta" state: light-aerobic metabolism, where desaturation and oxidation predominate. In this regime, the mechanism of survival is cell differentiation. The engine of these cells is mitochondrial oxidative phosphorylation, the fuel is HYDROGEN and the final acceptor is OXYGEN.

Cancer cells are in the "alpha" state, the most archaic of our evolution: darkness – anaerobic metabolism, where saturation and reducing state predominate. In this regime, the mechanism of survival is cell proliferation. The engine of these cells is the Embeden-Meyerhof cycle, the fuel is the HYDROGEN and the final acceptor the GSH.

At threat of death or severe injury, the cell discards the heavy beta state; discards the oxidative mechanism – aerobic metabolism – desaturation and passes to the simplest alpha state: anaerobic – reductive – proliferative metabolism. It is a state where electronic saturation predominates – the primitive state of survival.

According to this theory, already approved in experiments in vitro and in vivo, agents that favor electronic desaturation (electron acceptors) are highly effective substances in the treatment of cancer and benzaldehyde is just one of these substances. The electron acceptors preventing anaerobic glycolysis facilitate the structuring of cytoplasmic water.

Benzaldehyde abstracts electrons from various substances in the intracellular medium including GSH (reduced glutathione) by transforming it into GSSG (oxidized glutathione) which increases the cytoplasmic redox-oxidative potential, ie, benzaldehyde is an oxidizing agent.

Disulfiram, an aldehyde dehydrogenase inhibitor, potentiates the fall in GSH caused by acetaldehyde (Vina-1980) and possibly the same should occur with benzaldehyde. I mean, possibly disulfiram increases the effectiveness of benzaldehyde.

All substances that cause GSH to fall stimulate the activity of glucose-6-phosphate dehydrogenase (G6PD), as a defense mechanism, which increases the production of NADPH in an attempt to correct excess oxidation. This is the reason for the need to inhibit G6PD and the putative shunt transketolase to cause sustained oxidation and with it a sustained structuring of the cytoplasmic water and thus increase the effectiveness of this anticancer strategy. We can use, for example, DHEA plus genistein.

Many years ago, precisely in 1935, Dixon suggested that the presence of oxidizing agents could control cancer and Baker in 1937 demonstrated this hypothesis by finding that increased oxidized glutathione (GSSG) was able to inhibit anaerobic glycolysis.

In fact, when the intracellular medium is oxidizing, that is, the oxidation equilibrium tends towards oxidation, as GSSG (oxidized glutathione) is formed it inhibits anaerobic glycolysis. Inhibition of anaerobic glycolysis structures the cytoplasmic water, increases water type B, decreases entropy, increases the degree of order information of the cellular thermodynamic system and occurs stopping the proliferative cell cycle (mitosis), because the cell leaves the "near-death state". The consequence is the decrease of neoplastic cell proliferation with apoptosis of tumor cells. If oxidation is exaggerated, as in chemotherapy, we will have the catastrophic necrosis of tumor cells and normal cells (Felippe-2004-2008-2009).

When the redox potential is high, the intracellular type B water predominates and the cells remain in the quiescent stage, without proliferation. When the redox potential is high, ie when the intracellular medium is oxidizing, disulfide S-S bridges (eg GS-SG) and H-H hydrogen bonds are formed. These bridges stabilize the structure of enzymes, cell membrane, mitochondrial membrane, macromolecules, RNA and DNA. They stabilize the three-dimensional structure of the retinoblastoma protein (RBp) that remains dephosphorylated and therefore, the nuclear transcription necessary for the advancement of the cell cycle does not occur and the cells remain in the quiescent state without proliferation. Important fact is another effect of high redox potential. It inhibits the nuclear transcription factor NF-kappaB, which decreases cell proliferation, promotes apoptosis of the neoplastic cell and hinders tumor neoangiogenesis (Felippe- 1990-1994-2003-2004-2005). Perhaps the mechanism that is actually occurring is the need for activation of this strongly proliferative survival nuclear transcription factor because the cells have come out of the "near-death state" with the predominance of intracellular structured water.

If the intracellular medium is maintained oxidizing it is possible to block cell proliferation and the cell enters the G0 phase to then walk to apoptosis.

It is very interesting to know that the neoplastic cells require only a slight increase of the redox potential to cease proliferation, however this slight increase must be continuous and uninterrupted until apoptosis occurs, because if there is a fall in the redox potential,

the phosphorylation of the retinoblastoma protein And the cells proliferate again (Felippe-2004-2005).

Thus, the key to overcoming this fight is to keep the intracellular medium only mildly oxidizing for a sufficient period, ie to maintain the structuring of cytoplasmic water for a safe time for the cells to leave the "near-death state" which Kochi achieved with continued administration of benzaldehyde.

Leaving the "near-death state" the mechanisms of cell survival cease, the activation of oncogenes and cell signaling ceases and cells no longer need to proliferate to survive and can differentiate and walk to programmed death, without fanfare, without inflammation, to apoptosis.

Recently there have been numerous studies in experimental animals inoculated with cells of various types of human cancer and in culture of several types of human neoplastic cells, showing that the intracellular oxidizing medium causes cell cycle arrest and apoptosis by the following mechanisms:

a) Accumulation of p53 protein.
b) Activation of the caspase cascade.
c) Deoxyribonuclease activation.
d) Defphosphorylation of retinoblastoma protein.
e) Inhibition of protein tyrosine kinase (PTK).
f) Inhibition of Cdc25 phosphatase.
g) Inactivation of cdK1.
h) Decreased phosphofructokinase activity with decreased NADH.
i) Inhibition of Bcl-2 anti-apoptotic protein expression.
j) Inhibition of nuclear transcription factor NF-kappa-B.

These effects, directly explainable by the cancer cell's exit from the "near-death state", have been observed in more than 20 human cancers including: breast, prostate, lung, astrocytomas, gliomas, head and neck tumors, colorectal tumors, Tumors of the liver, pancreatic tumors, squamous cell carcinoma, etc. (Felippe 2004-2005).

Pettersen in 1983 shows that benzaldehyde inhibits neoplastic cell proliferation by interfering with the cell cycle. Inhibition of the G1, S and G2 phases of the cycle causes the mitosis to stop.

Benzaldehyde causes cytomorphological changes and cytotoxicity in cultured mammalian cells, compatible with inhibition of DNA synthesis (Nishimura-1981).

Four benzaldehyde derivatives showed potent antiproliferative activity in human glioblastoma multiforme cells at very small doses (Silva-2016).

In 1987, Masuyama shows that beta-cyclodextrin-benzaldehyde inhibits both spontaneous and experimental sarcoma pulmonary metastases. It suggests that benzaldehyde has direct effect on the tumor and indirectly on the cells "Natural Killer", immune system cells of capital importance. The following year, the same author showed inhibition of lung metastases in mice prone to cancer. Ochiai and Masuyama had already shown in 1986 that the inhibition of lung metastases in mice reached almost 100%, depending on the dose of benzaldehyde. Specifically the inhibition reached 73.8%, 85.6% and 95.7%, respectively, with doses of 0.5, 5 and 25mg per mouse per day.

Benzaldehyde was also shown to abolish the suppressive effect of fluoracil on "Natural killer" cells. Benzaldehyde increases lymphokine-activated killer cell activity activity of splenic cells, when together with interleukin-2 (Kuroki-1991).

In 1987, Kano revealed that benzaldehyde increases the thermo sensitivity of neoplasias and inhibits the dreaded tumor thermotolerance, which dramatically increases the efficacy of hyperthermia in the treatment of cancer.

In 2003, Li et al., studying a benzaldehyde derivative, clarify several points of its mechanism of action: it suppresses c-myc oncogene overexpression, inhibits Ras oncoprotein function, and increases p53 gene expression and interrupts P46 pathway associated with activation of mitosis, by mechanism other than the farnesylation of Ras protein.

Cobalt chloride reduces the cytotoxic activity of sodium ascorbate, curcumin and dopamine in oral tumor cells (HSC-2, HCG), but does not interfere with the effects of benzaldehyde (Sakagami-2000).

Dietary benzaldehyde and structurally related compounds inhibit the metabolism of nitrosamines, potent initiating agents and carcinogenesis promoters (Morse-1995). In this way benzaldehyde, a natural constituent of seeds and fruits is a cancer chemopreventive agent.

Another effect of benzaldehyde is as a potent partial and reversible inhibitor of the enzyme tyrosinase (Kubo-1999; Nihei-2004).

Myelogenous leukemia cells (HL-60, ML-1, KG-1) are the most sensitive to benzaldehyde-maltedextreine complex, CDBA, followed by epidermoid carcinoma cells (HSC-2, HSC-3, HSC-4) and Human glioblastoma (T98G, U87MG).

Benzaldehyde molecular targets

1. Hydrogen ion acceptor: mitotic motor block.
2. **Caution:** increases glucose-6-phosphate dehydrogenase activity by indirect and secondary effect as a defense mechanism against intracellular oxidation

– detrimental effect on cancer. Thus, when using benzaldehyde, we must inhibit G6PD, for example with DHEA or somatostatin.
3. Inhibits DNA synthesis.
4. Increases number and activity of Natural Killer cells.
5. Increases activity of LAK cells (Lymphokine-Activated Killer cells).
6. Increases the tumor thermosensitivity and prevents thermotolerance.
7. Suppresses overexpression of c-myc oncogene.
8. Inhibits the function of the Ras oncoprotein.
9. Increases p53 gene expression.
10. Interrupts pathway P46 of mitosis.
11. Inhibits tyrosinase.
12. Inhibits G1, S and G2 phases of the cell cycle.

Effect of benzaldehyde acting as oxidant

13. Increases p53 protein.
14. Activate caspase cascade.
15. Activates deoxyribonuclease.
16. Dephosphorylates and inhibitis retinoblastoma protein.
17. Inhibits protein tyrosine kinase.
18. Inhibits Cdc25 phosphatase.
19. Inhibits cdK1.
20. Inhibits MAP kinase.
21. Decreases phosphofructokinase activity with decreased NADH.
22. Inhibits Bcl-2 protein expression.
23. Inhibits NF kappa-B transcription: decreases neoplastic cell proliferation, increases apoptosis and decreases tumor neoangiogenesis

Amigdalin – Laetrile

Starting 1960 onwards, hundreds of people were treated in the United States and later in Mexico with Laetrile, a substance extracted from the inner amygdala of the apricot kernel. The effectiveness of Laetrile or amygdalin in patients with refractory cancer is around 30 to 50% in the various books consulted.

Amygdalin is composed of 1 molecule of benzaldehyde and a cyanide molecule and referred as vitamin B17. It was proven in 1980 that the active substance of the amygdalin was not cyanide, as it was thought for years, but benzaldehyde, a powerful and harmless oxidant.

Laetrile was heavily fought and then banned by the United States FDA, precisely because it contained cyanide in the molecule.

In PubMed, we find 302 references when in search we put "laetrile cancer" in April 2018.

Amigdalin molecular targets

1. **Caution:** Megadoses of ascorbic acid depletes GSH intracellularly and increases the risk of cyanide poisoning if administered with amygdalin (Calabrese-1979).
2. **Caution:** Many papers in the medical literature are on cyanide poisoning due to the use of amygdalin.
3. Inhibits NF-kappaB.
4. Inhibits COX-2.
5. Inhibits iNOS (inducible nitric oxide synthase).
6. **Gliomas**
   a) Amygdalin suppresses lipopolysaccharide-induced expression of cyclooxygenase-2 and suppresses iNOS (inducible nitric oxide synthase) in BV2 cells from murine microglia (Yang-2007).
   b) A 4-year-old child presented severe intoxication with intravenous amygdalin, orally plus the ingestion of apricot kernels for treatment of ependymoma. Improved with sodium thiosulfate (Sauer-2015).
7. **Lung cancer**
   a) Inhibits invasion of lung cancer H1299/M highly metastatic lineage and PA/M in vitro. There is extensive regulation of the expression of integrin and E-cadherin regulatory genes along the downstream side of the Akt/mTOR signaling pathway (Qian-2015).
8. **Breast cancer**
   a) It exerts cytotoxic activity on ER-positive breast cancer MCF-7 cells (Lee-2016).
9. **Triple negative breast cancer**
   a) Amygdalin increases apoptosis and adhesion in Hs578T and MDA-MB-231 cells of triple negative breast cancer. There is a decrease in Bcl-2 (B-cell lymphoma 2) associated with increased Bax, activation of caspase-3 with PARP (poly ADP-ribose polymerase) cleavage and activation of the pro-apoptotic molecule p38 MAPK (p38 mitogen-activated protein kinase) (Lee-2016).
10. **Prostate cancer**
    a) Induces apoptosis by regulating Bax and Bcl-2 in human prostatic cancer cells, DU145 and LNCaP (Chang-2006).
    b) Amygdalin slows the progression of the cell cycle and blocks the growth of prostatic cancer cells in castration-sensitive and DU-145 and PC3 (castration-resistant) cells. There is a decrease in proliferation in a dose-dependent manner. Apoptosis is reduced in PC3 and LNCap cells but not in DU-145, while colony formation is suppressed in all strains. The cycle

stops at G0/G1 due to modulation of the cell cycle proteins cdk1, cdk2 and cdk4 as well as cyclins A, B and D3 and p19 and p27 (Makarevic-2016).

11. **Liver cancer**
    a) Induces the expression of follistatin and inhibits the proliferation of HepG2 cells from hepatocellular carcinoma (Yang-2014).
12. **Colon cancer**
    a) Inhibits cell cycle genes and decreases the proliferation of colon cancer lineage, SNU-C4 (Parkk-2005).
13. **Uterus cervical cancer**
    a) Induces apoptosis in HeLa cells of human cervical cancer (Chen-2013).
14. **Leukemia**
    a) Induces apoptosis in human promyelocytic leukemia HL-60 cells (Kwon-2003).
15. **Bladder cancer**
    a) Blocks the growth of urinary bladder cancer lineage UMUC-3, RT112 and TCCSUP decreasing the expression of cyclin A and cdk2 (Makarevic-2014).
16. **Renal cancer**
    a) It blocks the invasion of renal carcinoma via integrins.
    b) Benzaldehyde in combination with irradiation os effective in renal cell carcinoma heterotransplanted in nude mice (Onishi-1986).
    c) Active products of benzaldehyde have activity agains renal cell carcinoma lines (Parise-2013).

Conclusion

As a substance that cannot be patented by the pharmaceutical industry, double blind and randomized studies were not invested.

Because it is non-toxic, benzaldehyde can be administered for a long time, maintaining a continuous and uninterrupted increase in the redox-oxidative potential, continuous and uninterrupted increase of type B structured water in the intracellular with all beneficial effects for the whole organism, besides the antitumoral effects.

After publishing this article on the website of the Brazilian Association of Biomolecular Medicine we received a letter from a oncology professor at the University of Montpellier, France, where he wrote that in the Catholic Bible was a report of possibly carcinomatous sores that healed only after the use of compresses of fig leaves, which we know to be rich in benzaldehyde.

To stop learning is to omit help. **JFJ**

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