# Laetrile for cancer: A systematic review of the clinical evidence

**Article** *in* Supportive Care in Cancer · July 2007

DOI: 10.1007/s00520-006-0168-9 · Source: PubMed



**3 authors**, including:

Stefania Milazzo

**14** PUBLICATIONS **832** CITATIONS

SEE PROFILE

Edzard Ernst

University of Exeter

**2,538** PUBLICATIONS **76,328** CITATIONS

SEE PROFILE

Support Care Cancer
DOI 10.1007/s00520-006-0168-9

REVIEW ARTICLE

**Stefania Milazzo**
**Stephane Lejeune**
**Edzard Ernst**

# Laetrile for cancer: a systematic review of the clinical evidence

Received: 19 July 2006
Accepted: 20 September 2006


S. Milazzo · E. Ernst (✉)
Complementary Medicine,
Peninsula Medical School,
Universities of Exeter and Plymouth,
Institute of Health and Social Care,
25 Victoria Park Road,
Exeter EX2 4NT, UK
e-mail: edzard.ernst@pms.ac.uk
Tel.: +44-1392-424989
Fax: +44-1392-427562

S. Lejeune
EORTC Data Centre,
Avenue E. Mounier 83, bte 11,
1200 Brussels, Belgium
e-mail: stephane.lejeune@eortc.be

**Abstract** *Background:* Many cancer patients treated with conventional therapies also try 'alternative' cancer treatments. Laetrile is one such 'alternative' that is claimed to be effective by many alternative therapists. Laetrile is also sometimes referred to as amygdalin, although the two are not the same. *Objective:* The aim of this review is to summarize all types of clinical data related to the effectiveness or safety of laetrile interventions as a treatment of any type of cancer. *Materials and methods:* All types of clinical studies containing original clinical data of laetrile interventions were included. We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (from 1951), EMBASE (from 1980), Allied and Complementary Medicine (AMED), Scirus, CancerLit, Cumulative Index to Nursing and Allied Health (CINAHL; all from 1982), CAMbase (from 1998), the MetaRegister, the National Research Register, and our own files. For reports on the safety of laetrile, we also searched the Uppsala database. No language restrictions were imposed. *Results:* Thirty six reports met our inclusion criteria. No controlled clinical trials were found. Three articles were nonconsecutive case series, 2 were consecutive case series, 6 were best case series, and 25 were case reports. None of these publications proved the effectiveness of laetrile. *Conclusion:* Therefore, the claim that laetrile has beneficial effects for cancer patients is not supported by sound clinical data.

**Keywords** Laetrile · Amygdalin · Cancer · Systematic review

## Background

Numerous surveys have reported that many people suffering from cancer turn toward so-called alternative cancer cures, i.e., unconventional treatments that are claimed to be effective either as a sole or concomitant therapy for cancer. "Alternative cancer cures" seem to be not supported by encouraging evidence, and some of them are associated with considerable risks [4]. The information currently available on the Complementary and Alternative Medicine (CAM) for Cancer Treatment has the potential to seriously mislead patients [5]. Many websites suggest a variety of "alternative cancer cures," and most of them advertise and sell such products (http://www.quackwatch.org/04ConsumerEducation/News/apricotseeds.html, cited 27 September 2004).

For about 40 years, laetrile has been one of the most popular "alternative cancer cures" [6]. Confusingly, laetrile is also sometimes called amygdalin, mandelonitrile beta-glucuronide [7], vitamin B17, bitter almond (http://www.curezone.com/foods/laetrile.html, cited 27 September 2004), mandelonitrile, apricot kernels, Xing Ren, amygdaloside, *Prunus armeniaca* (http://66.102.9.104/search?q=cache:i9d8wjzdGncJ:tcm.health-info.org/Herbology.Materia.Medica/xingren-properties.htm+amygdaloside+cancer+&hl=en, cited on 7 November 2004), nitriloside, *Prunus persica* seeds [8], *Prunus amygdalus* (http://www.1cure4cancer.com/controlcancer/information/laetrile.htm, cited 19 January

2005), Tao Ren or *Semen persica* (http://www.herbasin.com/database/taoren.htm, cited 27 September 2004), or prunasin (http://www.mskcc.org/mskcc/html/11571.cfm?RecordID=485&tab=HC, cited October 2004). Considerable confusion also exists concerning the relationship between the structure and nomenclature of laetrile and amygdalin. These names are often used interchangeably, although they do not describe the same product.

Amygdalin (Fig. 1) is a cyanogenetic glycoside plant compound [9] found in the pits of many fruits and in numerous plants belonging to the Rosaceae family such as *P. persica* (peach), *P. armeniaca* (apricot), *P. amygdalus* var. *amara* (bitter almond); it has also been found in the bark of *Prunus africana* (*pygeum*) [10], which is sometimes (wrongly) named bitter almond. Natural amygdalin has a dextrorotatory (*R*) configuration that is considered to be the active form [11]. Neo-amygdalin is its inactive (*S*) isomer and does not occur in nature; isoamygdalin (Fig. 2) is the name of the mixture of the epimers *R*-amygdalin and *S*-amygdalin [12].

The term 'laetrile' (Fig. 3) is an acronym from laevorotatory and mandelonitrile, used to describe a purified form of amygdalin [7, 8, 13]. The chemical composition of the US-patented laetrile (D-mandelonitrile-ß-glucuronide), a semisynthetic derivative of amygdalin, is different from the laetrile/amygdalin produced by Mexican manufacturers (D-mandelonitrile-ß-gentiobioside; Fig. 4) that is made from crushed apricot pits [7, 14].

Amygdalin was isolated by two French chemists, Robiquet and Boutron, and in 1837, it was named 'emulsin' by Liebig and Wöhler [14] (http://www.pasteur.fr/recherche/unites/REG/causeries/dates_1800.html, cited November 2004). In 1845, it was tried as a cancer treatment in Russia, and its first recorded use in the USA dates back to the 1920s (http://www.nci.nih.gov/cancertopics/pdq/cam/laetrile/healthprofessional/allpages, cited October 2004). In the 1950s, a purportedly nontoxic intravenous form of amygdalin was patented as laetrile. The results of an analysis conducted by the National Cancer Institute (NCI) of the purity of both oral and injectable amygdalin products manufactured by Cyto Pharma of Mexico indicated that these products did not comply with US pharmaceutical product standards [15]. Other analyses showed the presence of contaminants in both injectable and oral supplements of laetrile [14]. In spite of these concerns, many Americans continued to use laetrile so that the NCI decided to investigate its effectiveness. The results of their study failed to show anticancer activity: Of 22 cases, only 6 patients experienced a positive response [16]. In 1979, the Food and Drug Administration (FDA) ruled that laetrile products were toxic and ineffective, and laetrile was consequently banned [18]. In 1980, 23 US states legalized its use for terminal cancer patients [19, 20]. In the 1980s, two clinical trials were sponsored by the NCI with the approval of the FDA. Their results did not suggest laetrile to be effective. In 1987, Judge Bohanon issued an order effectively rendering the import of laetrile into the US as illegal [20]. Since then, laetrile has been banned in the USA and in Europe [21]. In the UK,

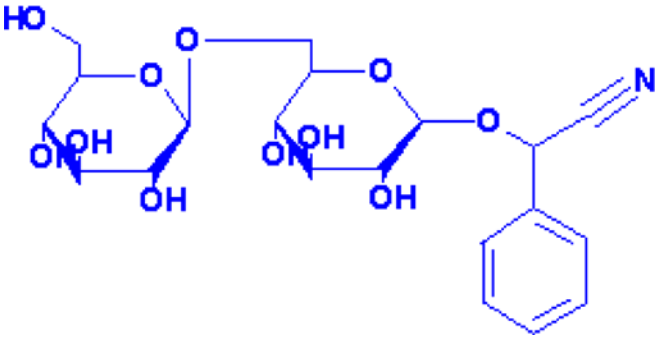


**Fig. 2** Isoamygdalin, C20-H27-N-011. This is the name of the mixture of the two epimers *R*-amygdalin and neo-amygdalin (*S*-amygdalin)

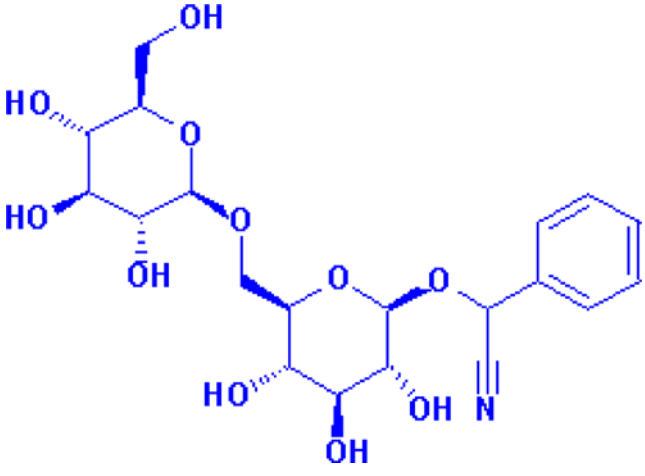


**Fig. 1** *R*-Amygdalin, C20-H27-N-011. It is a cyanogenetic glucoside. When cleaved by betaglucosidase, it releases at the first stage *R*-prunasin and a molecule of glucose

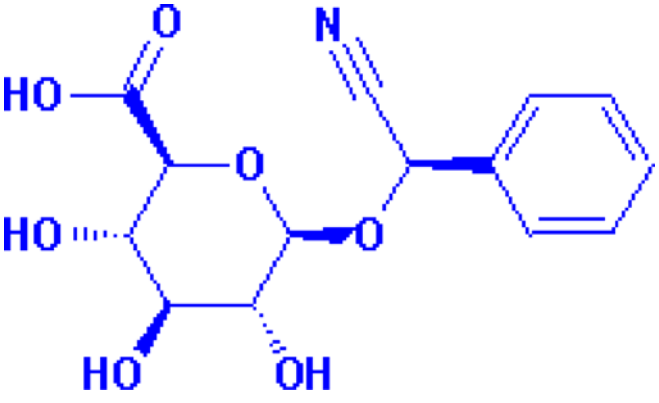


**Fig. 3** D-Mandelonitrile-ß-glucuronide or laetrile, C14-H15-N-07. This compound is similar to prunasin except for the COOH group that makes it a glucuronide rather than a glucoside

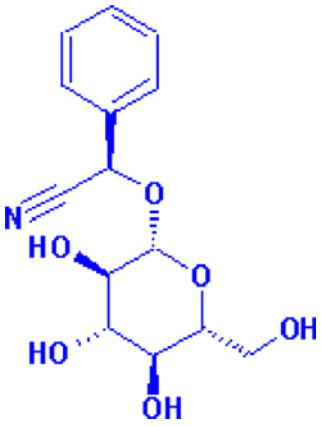


**Fig. 4** D-Mandelonitrile-ß-glucoside or D-mandelonitrile-ß-gentiobioside or prunasin is a cyanogenetic glycoside. When cleaved by prunasin beta-D-glucohydrolase in water, it releases glucose and mandelonitrile

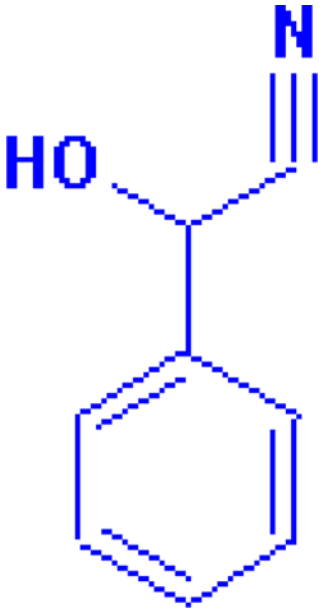


**Fig. 5** Mandelonitrile, C8-H7-N-O. In an aqueous solution, it may decompose spontaneously into benzaldehyde and HCN at a pH above 5, whereas the enzyme reaction also occurs at lower pH values

cyanogenetic substances are considered as "prescription medicine only" and can be prescribed under medical supervision only (http://medicines.mhra.gov.uk/ourwork/licensingmeds/legalstatus/lista.doc, cited 13 December 2004). Nevertheless, laetrile continues to be manufactured and administered as an anticancer therapy, primarily in Mexico [22]. Many websites are promoting and selling laetrile (http://www.quackwatch.org/04ConsumerEducation/News/apricotseeds.html, cited 27 September 2004), claiming, for instance, that the FDA has ruled laetrile as illegal to protect the profits of the pharmaceutical industry and permit testing on laetrile only by its opponents (http://www.cancertutor.com/WarBetween/War_Fda.html, cited 3 October 2004; http://www.u-magazine.com/magazine/articles.php?articleid=109, cited 3 October 2004).

Laetrile therapies are usually used alongside conventional cancer treatments or in combination with other unconventional methods such as metabolic therapy, urine therapy, diet therapy, fruit seeds intake (apricot, bitter almond, peach), oral supplements, and injections of betaglucuronidase [23]. Betaglucosidases enzymes found in intestinal bacteria [24] and in some commonly eaten plants break down laetrile and amygdalin to benzaldehyde, glucose, and cyanide (HCN) [14, 25], which is a constituent of mandelonitrile (Fig. 5). This is a structural component of both amygdalin and laetrile products, thought to be the active compound in laetrile products [26].

Laboratory studies have suggested anticancer effects of amygdalin [8, 11, 27–29]. Amygdalin and other cyanogenetic glucosides have been discussed as anticancer prodrugs [30, 31]. A Cochrane review found no randomized clinical trials (RCTs) of laetrile [32].

## Objectives

The aim of this review is to summarize any type of clinical evidence related to the effectiveness or safety of laetrile (or amygdalin interventions) in patients of all ages suffering from cancer of any type or stage. We wanted to go beyond the RCT evidence—not least because enthusiasts might argue that our Cochrane review [32] was too narrow to generate meaningful conclusions.

## Materials and methods

All types of human studies reporting original data of any kind of laetrile intervention for any cancer patient were considered for our systematic review. Studies on laetrile in any form such as oral supplements or parenteral (intravenous or intramuscular) were included. Since laetrile is used in combination with other therapies, such as 'metabolic therapy', we also included reports of laetrile use in combination with other treatments. In vitro and animal studies were excluded.

The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (from 1951), EMBASE (from 1980), Allied and Complementary Medicine (AMED), Scirus, CancerLit, Cumulative Index to Nursing and Allied Health (CINAHL; all from 1982), and CAMbase (from 1998) were searched. The MetaRegister (http://www.controlled-trials.com/) and the National Research Register (http://www.update-software.com/national/) were also searched. In addition, the bibliographies of all studies were scanned, and unpublished or on-going trials were identified through correspondence either with companies supplying or manufacturing laetrile or with clinics employing laetrile. For safety case reports, we searched the Uppsala database (Uppsala Safety Case Reports Database, https://websearch.who-umc.org, cited 1 June 2005). Finally, our own files were hand-searched. No language restrictions were imposed.

To search AMED, CINHAL, EMBASE, and MEDLINE, we used 'NHS dialog', a portal that provides the above-mentioned databases. MEDLINE was also searched

**Table 1** Search terms to identify the studies for this systematic review

| Database | Intervention(s) | Cancer patients | Types of study design | Location of studies |
|---|---|---|---|---|
| PubMed | 1. "Laetrile"/all MeSH | 18. Neoplasm* ti, ab, rw, sh. | 29. Clinical trial.pt. | 51. 17 AND 28 AND 50 |
| | 2. (((((Laetrile or laetril) or letril ) or letrile) or lactrile) or laetrile).ti.ab.sh.tw.rn. | 19. cancer*. ti, ab, rw, sh. | 30. controlled clinical trial.pt | |
| | 3. "amygdalin"/all MeSH | 20. carcin*. ti, ab, rw, sh. | 31 randomised controlled trial.pt | |
| | 4. ((((amygdalin or Neoamygdalin) or Amygdaloside) or isoamygdalin) or amygdaloside).ti.ab.sh.tw. | 21. oncol*. ti, ab, rw, sh. | 32. random*.tw | |
| | 5. ((((((mandelonitrile or mandelonitrile) or mandelonitrile (+−)-isomer) or mandelonitrile-beta-glucuronide) or Mandelonitrile-beta-gentiobioside) or Mandelonitrile beta gentiobioside) or Mandelonitrile beta glucuronic acid).ti.ab.sh.tw. | 22. sarcoman ti, ab, rw, sh. | 33. (double adj blind*).tw. | |
| | 6. (((mandelonitrile-beta-glucoside or prunasine) or prulaurasin) or prunasin (R)-isomer) | 23. tumor/all MeSH | 34. placebo*tw. | |
| | 7. Vitamin B 17 | 24. ((leucaemia or leukaemia) or leukemia) | 35. control*.tw. | |
| | 8. Prunus/all MeSH | 25. (adenoma or adenopathy) | 36. control*stud*.pt, tw. | |
| | 9. (((bitter almond or Prunus amygdalus) or Prunus amygdalus (semen or seeds)) or almond seeds) | 26. malignant. ti, ab, rw, sh. | 37. cohort stud*. pt, tw. | |
| | 10. (((Prunus armeniaca (semen or seeds) or Apricot (seeds or kernels)) or Xing Ren) or Semen Armeniacae amarum) | 27. Lymphoma. ti, ab, rw, sh. | 38. case-control stud*. pt, tw. | |
| | 11. ((((((Prunus persica (semen or seeds)) or Peach (semen or seeds)) or peach kernel) or semen (persica or pesicae)) or Tao Ren) or tonin) or tounin), | 28. or/18 – 27 | 39. human stud*. pt, tw. | |
| | 12. ((keishi-bukuryo-gan or keishibukuryogan) or TJ-25) | | 40. comparative study. pt, tw. | |
| | 13. nitriloside | | 41. follow-up stud*.pt, tw. | |
| | 14. sarcacinase | | 42. clinical stud*. pt, tw. | |
| | 15. C20-H27-N-O11(amygdalin) | | 43. case reports.pt | |
| | 16. C14-H15-N-O7 (laetrile) | | 44. toxicity.ab. | |
| | 17. or/1–16 | | 45. adverse event.ab. | |
| | | | 46. side effects.ab. | |
| | | | 47. death.ab. | |
| | | | 48. mortality.ab. | |
| | | | 49. stud*.ab. | |
| | | | 50. OR/29–49 | |
| NHS Dialog (AMED, CINHAL, EMBASE, MEDLINE) | All the terms where searched in the same way as above apart from the truncation symbol '*', which has been replaced by '$' followed by the number of possible letters | All the terms where searched in the same way as above apart from the truncation symbol '*', which has been replaced by '$' followed by the number of possible letters | All the terms where searched in the same way as above apart from the truncation symbol '*', which has been replaced by '$' followed by the number of possible letters | 51.17 AND 28 AND 50 |
| CAMbase | N/A | N/A | N/A | Laetrile for cancer; vitamin B17 for cancer; Amygdalin and cancer; Prunus and cancer |

through PubMed. All the search terms used to search PubMed were also used in NHS dialog (except for the truncation symbol '*' that was replaced by '$' in the latter; Table 1). To limit truncation and avoid the possibility of overflow, a number of characters after the wildcard also had to be specified.

All titles and abstracts were examined independently by the two reviewers. In case of discrepancies, the third author acted as an intermediator. Copies of potentially relevant articles were obtained. The eligibility of retrieved papers was assessed independently by the two reviewers. All articles were evaluated, and key data were extracted by the two reviewers according to predefined criteria: patient's age, sex and diagnosis, type of intervention and dosage, nature of adverse event and adverse effects, blood cyanide level [33], significant urine cyanide changes [34], use of prior conventional treatments, and clinical outcome.

## Results

Of the 64 articles retrieved through our searches, 36 articles met our inclusion criteria. The 28 excluded reports related to in vitro or animal studies or were not about cancer therapy (Fig. 6). No controlled clinical trials were found. Three articles reported nonconsecutive case series, 2 were consecutive case series (one of which was not published), 6 were best case series (series of case reports selected by the authors for the remarkably positive outcomes), and 25 were case reports (Tables 2 and 3).

A nonconsecutive case series [33] included six cancer patients and was designed as a pharmacological and toxicological study. Patients were administered both oral and intravenous laetrile together with "metabolic therapy" that included vitamins plus mineral preparations and pancreatin. Two patients were also given raw bitter almonds concomitantly with oral amygdalin. One patient who consumed raw almonds with laetrile experienced adverse events. No tumor regression or other beneficial results were reported.

The six patients from Moertel's study [33] were further analyzed, and 50–60 additional patients were given intravenous and oral amygdalin [34]. No hydrolysis of amygdalin to cyanide was noted, even with extremely high plasma concentration of the drug. No serious acute toxicity was encountered, and no tumor regression was reported.

Another nonconsecutive case series examined a population of 178 cancer patients [23], including the six patients of the previous study [33]. Patients received laetrile intravenously and orally at different dosages as adjunct to "metabolic therapy" (see above). Of the 153 symptomatic patients, 20% claimed subjective benefit at some time during therapy. One patient on oral laetrile and raw almond had symptoms characteristic of cyanide toxicity, which has also been observed in animal studies [35].

Tumor response and blood cyanide level (fatal when above 3 μg/ml) [33] were analyzed according to subgroups: oral laetrile vs intravenous laetrile, high-dose laetrile vs low-dose laetrile, and laetrile with other interventions (raw almonds) vs laetrile as sole intervention. Due to lack of essential data, these subgroup analyses are difficult to interpret. For instance, the comparison "high dose vs low dose" indicated a no dose–response relationship, although animal and human studies suggest that the toxicity of laetrile depends on the dosage and route of administration [33, 36]. High blood cyanide levels were noted in three patients who underwent low-dose therapy, and high blood cyanide levels were not documented in any patient receiving high-dose therapy. Oral administration is said to be associated with greater toxicity than intravenous, intraperitoneal, or intramuscular injection [25]. Yet of the 178 patients, 135 (76%) who had received intravenous laetrile experienced a toxic reaction, whereas 95 (72%) out of the 132 patients on oral laetrile experienced a toxic reaction, thus demonstrating a slightly higher toxicity among intravenously administered patients. No tumor

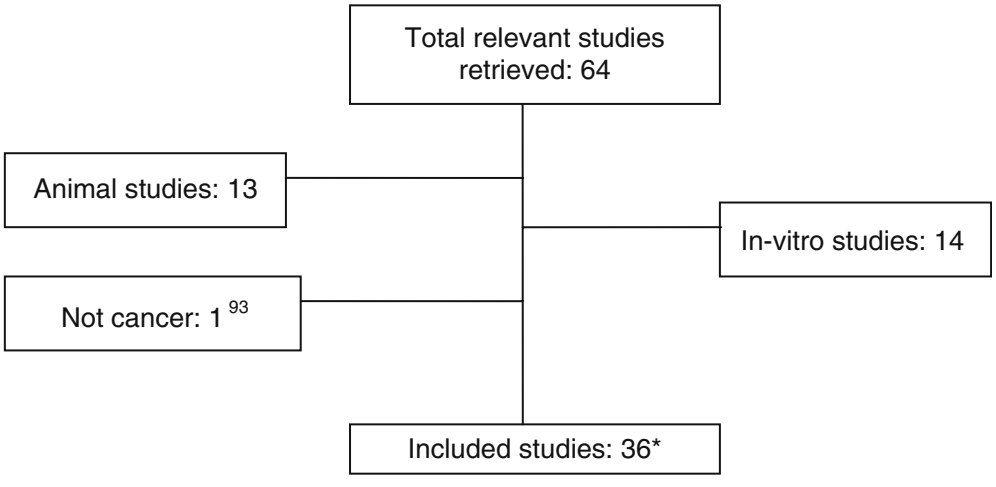


**Fig. 6** Flowchart of inclusion process. *Included studies: nonconsecutive case series, 3 publications; consecutive case series, 2 (1 is from an unpublished data); best case series, 6 publications; case reports, 25 publications

**Table 2** Results of clinical studies of laetrile for cancer

| First author (year) | Study design and follow-up | Sample size | Patient description | Name and type of intervention | Dosage | Duration | Primary outcome | Main results (n) | Adverse reaction reported (n) | Maximum blood HCN levels reported |
|---|---|---|---|---|---|---|---|---|---|---|
| Moertel (1981) [44] | Nonconsecutive case series | 6 | Any cancer<br>No other intervention prior laetrile treatment | L-Mandelonitrite-ß-D-glucuroniside-6-ß-glucoside | Low dose= 6 g/day | 21 days | Toxicity | Adverse events (1)<br>Slight rise of plasma thyocyanate level | Nausea, vomiting, vertigo, headache, heaviness | 2.01 µg/ml |
| | Not clearly stated | | Age, NS | Oral and intravenous | High dose= 7.5 g/day | | Pharmacology | No urinary cyanide excretion<br>No significant urinary thyocyanate excretion | | |
| Ames (1981) [45] | Nonconsecutive case series | 6 | Any cancer | D-Mandelonitrile-β-D-glucoside-6-ß-D-glucoside | NS | NS | Toxicity | Adverse events (1) | Cyanide toxicity symptoms | 2.1 µg/ml |
| | Not clearly stated | | No other intervention prior laetrile treatment<br>Age, NS | Oral and intravenous | | | Pharmacology | No amygdalin was detected in plasma samples<br>No urinary amygdalin excretion | | |
| Moertel (1982) [34] | Nonconsecutive case series | 178 | Any cancer | D-mandelonitrile-β-D-glucoside-6-ß-D-glucoside | Low dose= 6 g/day | NS | Toxicity | Adverse events (2) | Mental obtundation (1), dyspnea, nausea, vomiting, headache, dizziness, and dermatitis (1) | 3.1 µg/ml |
| | Not clearly stated | | No other intervention prior laetrile treatment | Oral and intravenous | High dose= 9 g/day | | Tumor response | Partial response (1) | | 3.5 µg/ml |
| | | | Age median=57 | | | | General condition | Symptomatic benefit (30.6) | | 3.7 µg/ml |
| CPW-Rahlstedt (1995) | Consecutive case series | 47 | Any cancer | Vitamin B17 | 3–12 g/day | Average= 37.3 days | Tumor response | Complete response (2) | Venous irritation (7), dizziness (2), flush (1), nausea (1), abdominal distention (1), fever (1) | NS |
| | NS | | Age average=55.6 | Intravenous | | | | Partial response (6)<br>Stable disease (15)<br>Progressive disease (9) | | |
| | | | | | | | Toxicity | Adverse events (13) | | |
| | | | | | | | General conditions | Symptomatic improvement (22) | | |
| Cancer commission (1953) [48] | Consecutive case series | 44 | Any cancer | Laetrile | NS | NS | Tumor response | Complete response (1) | NS | Not reported |
| | 6 months | | Age, NS | NS | | | | Stable disease (6)<br>Progressive disease (18) | | |

**Table 3** Results of best case series of laetrile for cancer

| First author (year) | Study design and follow-up | Sample size | Patient description | Name and type of intervention | Total dosage | Duration of treatment | Main results (n) | Adverse reaction reported (n) | Maximum blood cyanide levels reported |
|---|---|---|---|---|---|---|---|---|---|
| Guidetti (1955) [49] | Best case series<br>NS | NS | Colon, rectum, cervical, breast, pulmonary | Laetrile<br>Gauze, tampons drenched with laetrile solution | Up to 250 mg glucuroniside in 20 ml solution | 24-h application for 3 days | Tumors regression (NS) | High body temperature, shivering, sweating, fever, burning, sensation, discomfort (NS) | Not reported |
| Navarro (1957) [50] | Best case series<br>NS | 14 | Any cancer<br>Average age of 13 patients=42.5 | Laetrile<br>Iontophoresis injection | Average=2 g laetrile+1.9 g BG | Not clearly stated | Complete response (1)<br>Partial response (5)<br>Fetor reduction (3) | Vomiting (1), fever (2) | Not reported |
| Tasca (1959) [51] | Best case series<br>NS | 21 | Any cancer, not otherwise treatable<br>Average age of 20 patients=48.7 | L-Mandelonitrile-β-glicuronoside<br>Intravenous and local compress in some patients | Average for 20 patients=1.83 g | Not clearly stated | Partial response (9)<br>Stable disease (3)<br>Progressive disease (6) | Nausea (5), hemorrhage (2), jaundice (2), local pain after injection (2) | Not reported |
| Navarro (1964) [52] | Best case series<br>14 months, average for 4 patients | 5 | Any cancer<br>Average age=40.6 | Laetrile<br>Iontophoresis intravenous | Average for 4 patients=23.1 g | Average for 3 patients=62.3 days | Complete response (2) | None reported | Not reported |
| Navarro (1964) [53] | Best case series<br>NS for all patients | 9 | Adenocarcinoma, Hodgkin's disease, epidermoid carcinoma, hypernephroma, lymphorsarcoma, stomach | Laetrile<br>Intravenous | Average for 8 people=3.11 g (ranging from 2–15 g) | NS | Complete response (1)<br>Partial response (4)<br>Pain relief (7) | Pruritus (1)<br>Juandice (1) | Not reported |
| Morrone (1962) [54] | Best case series<br>NS | 10 | Average age=49.4<br>Breast, Hodgkin's disease, lung, prostate, pancreas, and omentum<br>Average age=44 | 1-mandelonitrile-β-glucuronoside<br>Intravenous | Average=46.2 g | Average=17.5 weeks | Parial response (8)<br>Pain relief (10)<br>Fetor reduction (1) | Fall of blood pressure followed by shock (1)<br>Burning and hitching (2) | Not reported |

NS: not specified

regression was observed in this study. One patient had a partial response for 10 weeks, but it was not specified which group this patient belonged to. A total of 95 patients showed progressive disease.

One uncontrolled trial was conducted in Japan in 1995 by CPW-Rahlstedt. This unpublished report was obtained by contacting laetrile manufacturers (Hospital of Anhui Medical University, 1995, unpublished report, "Summary of Clinical Efficacy of CDA-II"). It included 47 patients with various types of cancer undergoing cell differentiation agent II (CDA-II) therapy consisting of intravenous infusions of laetrile together with urine therapy, diet therapy, and vitamin C. Two complete responses were mentioned.

The Cancer Commission's study [37] is a case series that included 44 patients followed for 6 months. Some of the patients (no numbers were provided) experienced pain relief and an increase in well-being. This indicated, according to the authors, that laetrile might have exerted a temporary metabolic effect. One patient experienced complete remission but, as the authors pointed out, this could have been spontaneous.

Guidetti [38] reported on some patients (no exact number was provided) with various types of cancer treated with laetrile compresses applied locally to the affected area. Patients experienced tumor regression allegedly due to the lytic and destructive action of laetrile. However, because no numbers were provided, these data are uninterpretable.

Navarro [39] reported a case series with 14 patients with various types and stages of cancer. Patients were given different dosages of laetrile intravenously together with betaglucuronidase. The results suggested positive effects of laetrile on pain relief, appetite, reduction in odor of ulcerations, analgesia, weight gain, and tumor shrinkages in some cases. One patient allegedly had a complete response, but no follow-up was reported.

An Italian case series included 21 patients with advanced cancer [40]. Laetrile was given intravenously, and some patients were also treated with local compresses of laetrile solution. In some patients, normalizations of crythrocyte sedimentation rate and improvements of well-being were noted. Although, none of the patients had a complete response, survival rate was better than expected. The author concluded that laetrile was well tolerated and that pulmonary cancer was responsive to laetrile therapy. This report lacks crucial detail for a critical assessment.

In another case series, the outcomes were reported of five cancer patients treated with intravenous laetrile, sometimes together with betaglucosidase enzyme [41]. The patients experienced benefits after the therapy, and the author concluded that small doses of laetrile injected or administered by iontophoresis were particularly effective in early cases of metastasis (axilla) from surgically treated breast cancer. He also suggested that, in advanced cancer, laetrile could be better utilized at a dosage range of 3,000 up to 5,000 mg. Only two patients qualified as complete responses according to X-ray examinations.

The same author also reported positive outcomes for nine patients with different types of cancer in a best case series [42]. Patients were given laetrile intravenously or intramuscular with betaglucuronidase. One patient had a complete response with 7 months follow-up. Four other patients had a partial response, but follow-up data were provided in one case only. The author concluded that laetrile was likely to be an effective palliative treatment for advanced cases and speculated that it might even be curative in early cases. The lack of denominator data renders this report difficult to interpret.

Morrone [43] published a best case series of ten patients with different types of cancer treated with intravenous laetrile. All patients experienced pain relief. According to the authors, this was due to the benzoic acid given after laetrile. It is hydrolyzed by betaglucuronidase enzyme, which is thought to be highly concentrated in malignant lesions. Some patients experienced a reduction in adenopathy. No complete remissions were observed. Again, the lack of denominator data poses a problem.

Twenty-five case reports were found [44–68]. Laetrile was ineffective in five cases and effective in four cases. In three further cases, no clear outcome was indicated. Sixteen case reports reported adverse effects after laetrile administration in various forms and different dosages (Table 4). Among these 16 patients, two died because of adverse events due to cyanide poisoning. Seven additional toxicity case reports were excluded because they either referred to patients with diagnoses other than cancer or did not report in sufficient detail.

In total, our systematic review included 368 cancer patients, 14.4% of whom experienced adverse reactions mainly consisting of nausea, vomiting, headache, fever, and abdominal pain. Adverse events were usually associated with intravenous administration of laetrile, but they were also experienced by patients undergoing oral and intramuscular injections as well as enemas. No toxic effects of laetrile use in pregnant women were observed [42, 47].

To evaluate tumor response and symptomatic benefits, a total of 352 relevant cases are included in our systematic review; 3.1% of them allegedly had a complete response, 9.4% had a partial response, 6.8% had a stable disease, and 36.4% had tumor progression. Symptomatic benefits were reported in 22.9% of the cases. Due to the lack of denominators, these figures are likely to be biased.

## Discussion

This systematic review found no sound evidence that laetrile is effective as an anticancer agent. The claim that laetrile has anticancer effects is, therefore, not supported by data from controlled clinical trials. In a small number of reports, however, laetrile has been suggested to be of benefit

**Table 4** Results of case toxicity reports of laetrile for cancer

| First author | Type of cancer | Patient gender | Patient age | Name and type of intervention and dosage | Duration | Adverse events reported | Maximum blood cyanide level | Final outcome |
|---|---|---|---|---|---|---|---|---|
| Smith (1977) [78] | Lymphoma | Female | 48 | Laetrile (6 mg intravenously weekly+ 500 mg tablets 3 per day) | 2 months | Fever, malaise, headache, severe abdominal cramps, lymphadenopathy, hepatosplenomegaly | 1 mg/dl (10 μg/ml) | Recovered |
| | Lung and brain | Male | 46 | Laetrile (500 mg tablets one per day) | 6 months | Neuromuscular weakness | | Recovered |
| Sadoff (1978) [75] | Astrocytoma | Female | 17 | 10.5 g laetrile ampoules ingestion | 1 day | Headache, dizziness, collapse convulsions, labored breathing, dilated pupils, comatose, titanic contractures | Not reported | Dead |
| Ortega (1978) [74] | Kidney | Male | 2 | Laetrile (3.5 mg enemas daily) | 2 days | Vomiting, diarrhea | 214 μg/dl (2.14 μg/ml) | Recovered |
| Maxwell (1978) [73] | Sarcoma | Male | 69 | Laetrile (oral) | 1 year | Weakness, light-headedness, palpitations, headaches | 0.6 μg/dl (6 μg/ml) | Recovered |
| Morse (1979) [72] | Lung cancer | Female | 48 | Laetrile intravenous, intramuscular, oral, and rectal suppository routes daily | 9 days | Cold sweats, headaches, nausea, lethargy, dyspnea | 1.16 μg/ml | Recovered |
| Horwitz (1979) [71] | Acute lymphocitic leukemia | Male | 2 | Laetrile+vitamin C, enzyme enemas, and folic acid | NS | Cyanide poisoning | NS | Recovered |
| Rubino (1979) [70] | Nodular lymphoma | Female | 49 | Ingestion of 20–40 apricot pits | 1 day | Headache, weakness, disorientaion, nausea | 3.2 μg/ml | Recovered |
| Liegner (1981) [69] | Ductal carcinoma | Female | 61 | Laetrile (500-mg tablet twice a day) | 5 years | Fever, chill aches, malaise, agrunololcytosis | Not reported | Recovered |
| Vogel (1981) [68] | Breast carcinoma | Female | 57 | Laetrile[a] | NS | Comatose | 2.18 μg/ml | Dead |
| Uppsala database (1981) [78] | Malignant breast neoplasm | Female | 43 | Laetrile oral | NS | Rigors | NS | Recovered |
| Shragg (1982) [67] | Bowel carcinoma | Female | 67 | 5–12 bitter almonds[b] | 2 days | Light-headedness, nausea, vomiting, crampy abdominal pains, collapse | 2 μg/ml | Recovered |
| Kalynaraman (1983) [66] | Lymphoma | Female | 67 | 3 tablets of laetrile/ amygdalin daily | NS | Neuromyopathy | 191.8μg/100ml (191.8 μg/ml) | Recovered |
| Beamer (1983) [65] | Carcinoma | Male | 22 | 12–18 tablets of laetrile[c] | 1 day | Comatose, muscle rigidity | NS | Recovered |
| Leor (1986) [64] | Hepatoma | Female | 65 | Laetrile ampousles ingestion (9 g) | 2 days | Coma, hypotension, acidosis | 0.23 μg/ml | Recovered |
| Bromley (2005) [80] | Cancer | Female | 68 | Amygdalin 3 g concomitantly with vitamin C | 1 day | Seizure, reduced glasgow coma score, severe lactic acidosis | Not available | Recovered |

*NS* Not specified
[a]Patient had laetrile for a year.
[b]Patient had laetrile together with various drugs: Valium, Librium, stelazine, thorazine, dilantin, phenophen 3.
[c]Patient had also laetrile tablets daily for 6 months.

to cancer patients. It should be stressed again that, in the best case series and the case reports, the denominator, i.e., the number of cases treated, is not known. Therefore these types of reports may generate a false positive overall impression.

All positive results came from case reports and case series where subjective responses could erroneously be interpreted as objective evidence of efficacy. Many cases reporting tumor regression were referring to temporary regression and, in cases of alleged complete remission, none of the studies gave detailed information on follow-up. Some patients experiencing tumor regression might also have received conventional treatments. The nonconsecutive case series by Moertel [23] and the Cancer Commission [37] did not support the anticancer effect of laetrile and suggested laetrile to be toxic. The only unpublished study we found (CPW-Rahlstedt) suggested positive outcomes. This study lacks methodological details and was not peer-reviewed.

There are several reasons why the few allegedly positive results may, in fact, be 'false positives'. In particular, one should question whether patients actually had cancer to start with, whether the alleged benefit was due to laetrile or to concomitant treatments, and whether the outcome was real or assumed. None of the "positive" cases have been reported in sufficient detail to be sure on all these accounts. Furthermore, some of them were reported by authors who one might suspect of a conflict of interest.

In most of the studies, insufficient details were provided regarding chemical structure, brand name, extraction process, and purification methods. The name laetrile was often used interchangeably with amygdalin, vitamin B17, or other terminology. These names represent slightly different compounds with different pharmacological properties. Two nonconsecutive case series conducted by Moertel [33, 23] refer to L-mandelo-nitrile-ß-D-glucuroniside-6-ß-glucoside and D-mandelonitrile-ß-D-glucosido-6-ß-D-glucoside, respectively, but it is not clear whether the author used the wrong names or was referring to the actual reported ones. If so, the study published in 1982 [23] should not be considered as a follow-up of the previous one [33], because the two substances represent different compounds. On the other hand, the second study [23] included patients from the first [33]; thus, we suspect that Moertel et al. employed the wrong nomenclature. This exemplifies the importance of rational nomenclature for phyto-pharmaceuticals as the key to comparisons of activity, dosage, and price [69].

The risk of developing cyanide (HCN) poisoning after laetrile seems high and could increase with concomitant intake of fruit seeds (apricot, bitter almond, peach) [35], with megadoses of vitamin C [70], and in people with a genetically predisposed, diminished capacity to detoxify HCN [71]. Adverse events after laetrile intake could also be related to overdosing or to the quality of the products commercially available. Processing conditions are important factors affecting the quality of some *Rosaceae* seeds [72, 73], and often, laetrile/amygdalin preparations come from questionable sources. Those preparations could be mutagenic [7] or could contain bacteria [15] or other contaminants and impurities [14]. Other preparations may contain only mandelonitrile glucuronide or various concentrations of amygdalin and isoamygdalin, or may contain no glucuronide at all [7].

Not only is the evidence that laetrile does more good than harm weak, but also the plausibility of its postulated mode of action is debatable. Two theories claim that malignant cells are deficient in rhodanese enzyme and have abnormal levels of betaglucuronidase and betaglucosidase, enzymes responsible for the breaking down of laetrile and amygdalin, respectively (http://www.nci.nih.gov/cancertopics/pdq/cam/laetrile/healthprofessional/allpages, cited October 2004) [74]. Rhodanese can convert cyanide into the relatively harmless compound thyocyanate [9] when laetrile is broken down by the betaglucuronidase, producing cyanide. This would affect cancer cells more than healthy ones. However, there is no experimental evidence to show that malignant and healthy cells differ in rhodanese enzymes [75] nor that betaglucosidase is contained in tumor tissues [27]. High levels of betaglucuronidase have been noted in the tissue, blood serum, and urine of cancer patients [76, 77], so that drugs, such as 1-mandelonitrile-glucuronide, may selectively release cyanide to tumor tissues [27]. A third theory refers to cancer as a metabolic disorder and proposes that cancer develops due to the deficiency of a vitamin, named vitamin B17, which has been described indifferently as amygdalin and laetrile (http://www.curezone.com/foods/laetrile.html, cited 27 September 2004) [78]. Although some (but by no means all) studies suggest a beneficial effect of vitamins in cancer therapy [79], there is no evidence that laetrile is a vitamin, that cancer is a metabolic disease, or that lack of laetrile is involved in carcinogenesis [80]. A fourth theory suggests that cyanide leads to the disruption of lysosomes by increasing the acid content of cancer cells, and that the lysosomes release their enzyme content, which causes the death of cancer cells (http://www.nci.nih.gov/cancertopics/pdq/cam/laetrile/healthprofessional/allpages, cited October 2004). Cyanide can kill cancer cells by diffusing through the cell membrane and inhibiting mitochondrial respiration [30]. It could also be useful as a "radio sensitizer", improving the effect of radiotherapy in cancer cells [27] (http://ott.od.nih.gov/db/abstxt.asp?refno=148, cited 2 February 2005). However, its cytotoxic activity could also affect healthy cells [30]. A theory promoted by an unpublished document provided by a laetrile supplier (CPW-Rahlstedt) claims that laetrile is formed in the body after amygdalin administration. According to this theory, amygdalin is transformed in the liver and kidneys into glucose and mandelonitrile, which subsequently would combine with glucuronic acid to produce laetrile. No experimental evidence has been found in the literature to support this theory. In view of recent promising laboratory

studies on the anticancer effect of amygdalin [8, 11, 31], future investigations might be considered–if only to put the patient's mind at rest.

Our review has several limitations. The quality and paucity of data limits the conclusiveness of our findings. Although our searches were extensive, we cannot be certain that they retrieved all the available evidence. The studies we combined in this analysis had different methodological designs and related to various forms of cancer with different etiologies. This heterogeneity renders the interpretation of the evidence difficult.

In conclusion, there is no reliable evidence for the effectiveness of laetrile, and considerable doubt about its safety exists. The risk–benefit balance of laetrile as a treatment for cancer is therefore negative. Well-designed, controlled clinical trials to test laetrile or amygdalin could be considered.

**Acknowledgement** The authors thank Katja Schmidt for her valuable support and the European Commission for having funded the CAM-Cancer project within its fifth framework program.

## References


1. http://www.who.int/cancer/media/en/788.pdf
2. http://216.239.59.104/u/who?q=cache:Pqq2bFQPilgJ:www.euro.who.int/childhealthenv/Risks/CancerTop+children+cancer&hl=en&ie=UTF-8
3. http://www.cancer.org/docroot/CRI/content/CRI_2_4_1X_Introduction_7.asp?sitearea
4. Gibbs M (2004) Networking topics for palliative care. Pharm J 273(7320):539
5. Schmidt K, Ernst E (2004) Assessing websites on complementary and alternative medicine for cancer. Ann Oncol 15:733–742
6. Holland JC (1982) Why patients seek unproven cancer remedies: a psychological perspective. CA Cancer J Clin 32(1):10–14
7. Fenselau C, Pallante S, Batzinger RP, Benson WR, Barron RP, Sheinin EB, Maienthal M (1977) Mandelonitrile beta-glucuronide: synthesis and characterization. Science 198 (4317):625–627
8. Fukuda T, Ito H, Mukainaka T, Tokuda H, Nishino H, Yoshida T (2003) Anti-tumor promoting effect of glycosides from *Prunus persica* seeds. Biol Pharm Bull 26(2):271–273
9. Jean Bruneton (1999) Pharmacognosy, 2nd edn. Intercept, Paris
10. Gurib-Fakim A, Brendler T (2004) Medicinal and aromatic plants of Indian Ocean islands. Medpharm, Stuttgart, Germany
11. Kwon HY, Hong SP, Hahn DH, Kim JH (2003) Apoptosis induction of *Persicae Semen* extract in human promyelocytic leukemia (HL-60) cells. Arch Pharm Res 26(2):157–161
12. Turczan JW, Medwick T, Plank W (1978) Cyanogenetic glycosides. J Assoc Off Anal Chem 61:192–207
13. Howard-Ruben J, Miller NJ (1984) Unproven methods of cancer management. Part II: current trends and implications for patient care. Oncol Nurs Forum 11(1):67–73
14. Dorr RT, Paxinos J (1978) The current status of laetrile. Ann Intern Med 89 (3):389–397
15. Davignon JP, Trissel LA, Kleinman LM (1978) Pharmaceutical assessment of amygdalin (laetrile) products. Cancer Treat Rep 62(1):99–104
16. Ellison NM, Byar DP, Newell GR (1978) Special report on laetrile: NCI (National Cancer Institute) laetrile review. N Engl J Med 299:549–552
17. David Shaffer (1979) The Associated Press (July 16)
18. Michael Putzel (1979) The Associated Press (June 19)
19. 23 states have passed laetrile legislation (1980) The Associated Press (December 21)
20. Curran WJ (1980) Law-medicine notes. Laetrile for the terminally ill: Supreme Court stops the nonsense. N Engl J Med 302(11):619–621
21. Meijer EL (2001) Sale over the Internet of substances for human consumption which are regarded as harmful in America. Off J (2001/C 151 E/071)
22. Questionable cancer practices in Tijuana and other Mexican border clinics (1991). CA Cancer J Clin 41 (5):310–319
23. Moertel CG, Fleming TR, Rubin J, Kvols LK, Sarna G, Koch R, Currie VE, Young CW, Jones SE, Davignon JP (1982) A clinical trial of amygdalin (laetrile) in the treatment of human cancer. N Engl J Med 306(4):201–206
24. Carter JH, McLafferty MA, Goldman P (1980) Role of the gastrointestinal microflora in amygdalin (laetrile)-induced cyanide toxicity. Biochem Pharmacol 29(3):301–304
25. Newmark J, Brady RO, Grimley PM, Gal AE, Waller SG, Thistlethwaite JR (1981) Amygdalin (laetrile) and prunasin beta-glucosidases: distribution in germ-free rat and in human tumor tissue. Proc Natl Acad Sci U S A 78 (10):6513–6516
26. Miller KW, Anderson JL, Stoewsand GS (1981) Amygdalin metabolism and effect on reproduction of rats fed apricot (*Prunus armeniaca*) kernels. J Toxicol Environ Health 7(3–4):457–468
27. Biaglow JE, Durand RE (1978) The enhanced radiation response of an in vitro tumour model by cyanide released from hydrolysed amygdalin. Int J Radiat Biol Relat Stud Phys Chem Med 33(4):397–401
28. Manner HW, Di Santi SJ, Maggio MI (1978) Amygdalin, vitamin A and enzyme induced regression of murine mammary adenocarcinomas. J Manip Physiol Ther 1(4):246–248
29. Bhatti RA, Ablin RJ, Guinan PD (1981) Tumour-associated directed immunity in prostatic cancer: effect of amygdalin. IRCS Med Sci Clin Biochem 9(1):19

30. Kousparou CA, Epenetos AA, Deonarain MP (2002) Antibody-guided enzyme therapy of cancer producing cyanide results in necrosis of targeted cells. Int J Cancer 99(1):138–148 (May 1)
31. Syrigos KN, Rowlinson-Busza G, Epenetos AA (1998) In vitro cytotoxicity following specific activation of amygdalin by beta-glucosidase conjugated to a bladder cancer-associated monoclonal antibody. Int J Cancer 78 (6):712–719
32. Milazzo S, Ernst E, Lejeune S, Schmidt K (2006) Laetrile treatment for cancer. The Cochrane Database of Systematic Reviews, Issue 2, Art. No.: CD005476
33. Moertel CG, Ames MM, Kovach JS, Moyer TP, Rubin JR, Tinker JH (1981) Pharmacologic and toxicological study of amygdalin. JAMA 245(6):591–594 (Feb 13)
34. Ames MM, Moyer TP, Kovach JS, Moertel CG, Rubin J (1981) Pharmacology of amygdalin (laetrile) in cancer patients. Cancer Chemother Pharmacol 6(1):51–57
35. Schmidt ES, Newton GW, Sanders SM, Lewis JP, Conn EE (1978) Laetrile toxicity studies in dogs. JAMA 239 (10):943–947 (Mar 6)
36. McAnalley BH, Gardiner TH, Garriott JC (1980) Cyanide concentrations in blood after amygdalin (laetrile) administration in rats. Vet Hum Toxicol 22 (6):400–402 (Dec)
37. Treatment of cancer with laetriles; a report by the Cancer Commission of the California Medical Association (1953). Calif Med 78(4): 320–326 (Apr)
38. Guidetti Hector (1955) Observations preliminaries sur quelques cas de cancer traits par un glycuronosyde cyanogenetique. Acta XI(2):156–158
39. Navarro MD (1957) The mechanism of action and therapeutic effects of laetrile in cancer. J Philipp Med Assoc 33 (8):620–627
40. Tasca M (1959) Clinical observations on the therapeutic effects of a cyanogenetic glycuronoside in cases of human malignant neoplasms. Gazz Med Ital 118(4):153–159 (Apr)
41. Navarro MD (1964) Laetrile therapy in cancer. Acta Unio Contra Cancrum 20:392–394
42. Navarro MD (1959) Five years experience with laetrile therapy in advanced cancer. Five years experience with laetrile therapy in advanced cancer. Acta Unio Int Contra Cancrum 15 (Suppl 1):209–221
43. Morrone JA (1962) Chemotherapy of inoperable cancer: preliminary report of 10 cases treated with laetrile. Exp Med Surg 20:299–308
44. Helvie CO, Cayce CT (1997) Alternative treatment for lung cancer and irregular heartbeat: two case studies. Alternate Health Pract 3(3):185–194
45. Quackery PP (1992) South Med J 85 (2):1264
46. Mehta P (1980) Ineffectiveness of laetrile in the treatment of acute lymphoblastic leukemia. Clin Pediatr (Phila) 19(5):363–364 (May)
47. Perspective: resolving an ethical dilemma (1980). Nursing 10(5):39–43
48. Peterson RG, Rumack BH (1979) Laetrile and pregnancy. Clin Toxicol 15 (2):181–184
49. Campbell DR, Mason WF, Standen JR (1978) Renal arteriography in von Hippel–Lindau disease. J Can Assoc Radiol 29(4):243–246 (Dec)
50. Ames MM, Kovach JS, Flora KP (1978) Initial pharmacologic studies of amygdalin (laetrile) in man. Res Commun Chem Pathol Pharmacol 22 (1):175–185 (Oct)
51. Reactions to "laetrilomania" (1977). N Engl J Med 297(4):218–221 (Jul 28)
52. Crippen DW, Veatch RM (1976) Laetrile: cancer cure or quack remedy? Hastings Cent Rep 6(6):18–20 (Dec)
53. Leor R, Michaeli J, Brezis M, Stessman J (1986) Laetrile intoxication and hepatic necrosis: a possible association. South J Med 79(2):259–260 (Feb)
54. Beamer WC, Shealy RM, Prough DS (1983) Acute cyanide poisoning from laetrile ingestion. Ann Emerg Med 12 (7):449–451 (Jul)
55. Kalyanaraman UP, Kalyanaraman K, Cullinan SA, McLean JM (1983) Neuromyopathy of cyanide intoxication due to "laetrile" (amygdalin). A clinicopathologic study. Cancer 51 (11):2126–2133 (Jun 1)
56. Shragg TA, Albertson TE, Fisher CJ Jr (1982) Cyanide poisoning after bitter almond ingestion. West J Med 136 (1):65–69 (Jan)
57. Vogel SN, Sultan TR, Ten Eyck RP (1981) Cyanide poisoning. Clin Toxicol 18(3):367–383 (Mar)
58. Liegner KB, Beck EM, Rosenberg A (1981) Laetrile-induced agranulocytosis. JAMA 246(24):2841–2842 (Dec 18)
59. Rubino MJ, Davidoff F (1979) Cyanide poisoning from apricot seeds. JAMA 241(4):359 (Jan 26)
60. Horwitz ET (1979) Of love and laetrile: medical decision making in a child's best interests. Am J Law Med 5 (3):271–294
61. Morse DL, Boros L, Findley PA (1979) More on cyanide poisoning from laetrile. N Engl J Med 301(16):892 (Oct 18)
62. Maxwell DM (1978) Increased cyanide values in a laetrile user. Can Med Assoc J 119(1):18 (Jul 8)
63. Ortega JA, Creek JE (1978) Acute cyanide poisoning following administration of laetrile enemas. J Pediatr (6):1059 (Dec)
64. Sadoff L, Fuchs K, Hollander J (1978) Rapid death associated with laetrile ingestion. JAMA 239(15):1532 (Apr 14)
65. Smith FP, Butler TP, Cohan S, Schein PS (1977) Laetrile toxicity: a report of two cases. JAMA 238(13):1361
66. Navarro MD (1955) Metastatic pulmonary carcinoma treated with laetrile. Unitas 28:606–618
67. Navarro MD, Lagman CL (1957) Breast carcinoma with lung and bone metastases treated with laetrile; case report. J Philipp Med Assoc 33(1):16–20 (Jan)
68. Bromley J, Hughes BG, Leong DC, Buckley NA (2005) Life-threatening interaction between complementary medicines: cyanide toxicity following ingestion of amygdalin and vitamin C. Ann Pharmacother 39(9):1566–1569 (Sep)
69. Bonati A (1991) How and why should we standardize phytopharmaceutical drugs for clinical validation? J Ethnopharmacol 32(1–3): 195–197 (Apr)
70. Calabrese EJ (1979) Conjoint use of laetrile and megadoses of ascorbic acid in cancer treatment: possible side effects. Med Hypotheses 5(9):995–997 (Sep)
71. Calabrese EJ (1979) Possible side effects from treatment with laetrile. Med Hypotheses 5(9):1045–1049 (Sept)
72. Hwang EY, Lee JH, Lee YM, Hong SP (2002) Reverse-phase HPLC separation of D-amygdalin and neoamygdalin and optimum conditions for inhibition of racemization of amygdalin. Chem Pharm Bull (Tokyo) 50(10):1373–1375 (Oct)
73. Hu S, Yuan D, Diao GF, Bi KS, Kano Y (2002) Studies on evaluation of *Semen Armeniacae amarum*. Zhongguo Zhong Yao Za Zhi 27(10):736–739 (Oct)

74. Krebs ET Jr, Krebs ET Sr, Beard HH (1950) The unitarian or trophoblastic thesis of cancer. Med Rec 163(7):149–174
75. Gal EM, Fung FH, Greenberg DM (1952) Studies on the biological action of malononitriles, II: distribution of rhodanese (transulfurase) in the tissues of normal and tumor-bearing animals and the effect of malononitriles thereon. Cancer Res 12:574–579
76. Conchie J, Findlay J, Levvy GA (1959) Mammalian glycosidases: distribution in the body. Biochem J 71(2):318–325
77. Fishman WH (1955) Beta-glucoronidase. Adv Enzymol Relat Subj Bioch 16:361–409
78. Krebs ET Jr (1970) The nitrilosides (vitamin B17)—their nature, occurrence and metabolic significance antineoplastic vitamin B17. J Appl Nutr 22:75–86
79. Donaldson MS (2004) Nutrition and cancer: a review of the evidence for an anti-cancer diet. Nutr J 3(1):19 (Oct 20)
80. Young VR, Newberne PM (1981) Vitamins and cancer prevention: issues and dilemmas. Cancer 47(Suppl 5):1226–1240 (Mar 1)
81. Sakamoto S, Yoshino H, Shirahata Y, Shimodairo K, Okamoto R (1992) Pharmacotherapeutic effects of kuei-chih-fu-ling-wan (keishi-bukuryo-gan) on human uterine myomas. Am J Chin Med 20(3–4):313–317