The aetiology, prevalence and morbidity of outbreaks of photosensitisation in livestock: A review

Yuchi Chen[^1,2], Jane C. Quinn[^1,2*], Leslie A. Weston[^2,3], Panayiotis Loukopoulos[^1,2,4]

[^1,2,3,4]: School of Animal and Veterinary Sciences, Charles Sturt University, Wagga Wagga, New South Wales, Australia, 2 Graham Centre for Agricultural Innovation, Charles Sturt University and NSW Department of Primary Industries, Wagga Wagga, New South Wales, Australia, 3 School of Agriculture and Wine Science, Charles Sturt University, Wagga Wagga, New South Wales, Australia, 4 Melbourne Veterinary School, University of Melbourne, Werribee, Victoria, Australia

[^*]: jquinn@csu.edu.au

Abstract

**Background**

Photosensitisation is a clinical condition occurring in both humans and animals that causes significant injury to affected individuals. In livestock, outbreaks of photosensitisation caused by ingestion of toxic plants are relatively common and can be associated with significant economic loss.

**Objectives**

The agents that are most commonly implicated in outbreaks of photosensitisation have not been formally investigated on a global scale. To address this question, a systematic review of the literature was undertaken to determine the most common causative agents implicated in outbreaks of photosensitisation in livestock in Australia and globally, as well as the prevalence and morbidity of such outbreaks.

**Methods**

A systematic database search was conducted to identify peer-reviewed case reports of photosensitisation in livestock published worldwide between 1900 and April 2018. Only case reports with a full abstract in English were included. Non peer-reviewed reports from Australia were also investigated. Case reports were then sorted by plant and animal species, type of photosensitisation by diagnosis, location, morbidity and mortality rate and tabulated for further analysis.

**Results**

One hundred and sixty-six reports qualified for inclusion in this study. Outbreaks were reported in 20 countries. Australia (20), Brazil (20) and the United States (11) showed the highest number of peer-reviewed photosensitisation case reports from this analysis. Hepatogenous (Type III) photosensitisation was the most frequently reported diagnosis (68.5%)
and resulted in higher morbidity. *Panicum* spp., *Brachiaria* spp. and *Tribulus terrestris* were identified as the most common causes of hepatogenous photosensitisation globally.

**Conclusions**

Hepatogenous photosensitisation in livestock represents a significant risk to livestock production, particularly in Australia, Brazil, and the United States. Management of toxic pastures and common pasture weeds may reduce the economic impact of photosensitisation both at a national and global level.
other toxic entities, and the relative dearth of information on their biochemical profile commonly makes confirmation of a definitive causal agent problematic.

Several reviews of the incidence and prevalence photosensitisation in livestock have been published [1,4,26–31]. However, these have either focused on summarisation of diagnostic criteria [1,8,27,31,32], emphasised particular aetiological agents or been restricted to certain geographical regions [3,4,26,28,33]. As such, although providing useful information to the clinician or epidemiologist, they are generally limited in their ability to determine outbreak patterns, the prevalence of the causative agents, their relationship to morbidity, and the mortality on a larger scale. The lack of a holistic approach to the study of photosensitisation therefore limits our understanding of its impact on livestock globally.

The objective of this study was, therefore, to review the global presentation of cases of photosensitisation in the scientific literature, published in the English language, and to determine potential trends in which causal agents worldwide that are most commonly associated with outbreaks of photosensitisation in livestock. A review of the literature, including both peer-reviewed and non peer-reviewed sources, was undertaken for a better understanding of photosensitisation across a number of key countries globally where a significant body of published case information could be obtained.

Methods

Database analysis, search, and selection criteria: Peer-reviewed articles

Eleven electronic databases [Pubmed, Web of Science, CAB Abstracts, Proquest, Sciquest, Trove, EthOS, BASE, Open Access and Dissertations, NDLTD, and the DART Europe E Theses Portal] were mined for peer-reviewed articles relating to cases of photosensitisation in livestock. All case reports were extracted regardless of year or language of publication. Searches included the period from 1900 to April 2018. Search keywords included ‘photosensitisation’ and / or ‘photosensitization’, ‘photodermatitis’, ‘facial eczema’, ‘geeldikkop’, ‘dikoor’, ‘plochteach’ or ‘alveld’ in the title. The Boolean operator “OR” was used to join terms. Language restriction was applied; articles published in languages other than English, or did not provide an abstract in English, were excluded from the search result. Reference lists of retrieved articles were reviewed to identify all relevant case studies or reports to maximise article retrieval. The PRISMA checklist is attached as Supporting Checklist.

The following selection criteria were then applied; the publication should: 1) be an outbreak report with photosensitisation as the main clinical sign or differential diagnosis; 2) relate to any species of livestock, including alpaca, camel, cattle, deer, donkey, goat, horse, llama, mule, pig, reindeer, sheep, and water buffalo; and 3) contain clinicopathological findings that confirm a diagnosis of photosensitisation. Quality assessment of individual peer-reviewed reports was not performed. In particular, an assumption made with respect to the peer reviewed articles was that the causal agent responsible for all reported outbreaks were correctly identified in the associated publication.

Exclusion criteria included: duplications of published articles; species other than domestic livestock; publications in which the full text or a detailed abstract was not available; and publications in which the diagnosis of photosensitisation could not be established over other differentials. Search and selection methodology for this study is summarised in Fig 1.

Database analysis, search, and selection criteria: Non peer-reviewed articles

Although the reliability of the diagnosis and the utility of information in non-peer reviewed reports can sometimes be questionable, it was considered that non peer-reviewed reports could be useful as supplemental information to peer-reviewed data by providing careful data
extraction and thus review of the evidence in each report was undertaken. Australia was selected as the sole country for analysis of non peer-reviewed information due to its well-established case reporting systems via Australian Government Administrative or Government-Accredited Animal Health Officers (District Veterinarians, Regional Veterinary Officers, and Biosecurity Officers). Reports from these sources are published either in Animal Health Surveillance Quarterly Report (AHSQR, http://www.sciquest.org.nz/ahsq) that cover outbreaks
nationally in Australia, or in the ‘Flock and Herd’ case note series that cover outbreaks in New South Wales (NSW) (F&H, http://www.flockandherd.net.au, site maintained by Local Land Services in NSW). Non peer-reviewed case material was searched up to and including April 2018. Again, the same selection and exclusion criteria were applied as described above.

Extracted information from non peer-reviewed case reports included, but was not limited to, species; age; quantitative and qualitative information regarding proportion of the herd or flock affected; geographical and chronologic information; type of photosensitisation and clinical description; causative agents confirmed or suspected. The accuracy of the diagnosis and entirety of the report was reviewed by the authors to ensure consistency, and reports, where clinicopathological data or causality did not appear consistent with a diagnosis of photosensitisation, were excluded from the analysis. However, due to the lack of peer-reviewed process, the accuracy and reliability of non peer-reviewed reports were considered to represent a lower level of evidence than peer-reviewed ones.

Results

Following review of the peer-reviewed scientific literature, 78 reports presenting with a full text or detailed abstract were analysed (Fig 1). Data on causal plant species or organisms; geographical location; type of photosensitisation (primary, hepatogenous, congenital, unknown); outbreak years; animal species; size of flock or herd, percentage of morbidity and mortality were extracted and tabulated. A summary of information presented in the peer-reviewed literature is shown in Table 1.

Following review of the Australian non peer-reviewed scientific literature, 88 non peer-reviewed Australian case reports with a full text or detailed abstract were identified for further review. Data on causal plant species or organism, country of outbreak, type of outbreak related to type of photosensitisation (primary, hepatogenous, congenital, unknown), animal species, size of flock or herd and percentage morbidity and mortality was extracted. Data contained in these reports was often less comprehensive than comparative peer-reviewed articles and information on the above criteria were extracted where available. A summary of information presented in Australian non peer-reviewed literature is shown in Table 2.

Geographical distribution and species differentiation of photosensitisation outbreaks reported in the peer-reviewed literature

Photosensitisation outbreak reports were identified from 20 different countries in the peer-reviewed literature (Fig 2). The greatest number of reports were from Australia (20), Brazil (20), and the United States (11), followed by New Zealand (7), United Kingdom (7), South Africa (4), Iran (4), Norway (2), Turkey (2) and Malaysia (2), and 10 other countries with only one outbreak report each.

A prominent species predisposition was identified in these reports. Sheep were the most reported species in photosensitisation outbreaks globally, with 47.2% (42/89) reported outbreaks, followed by cattle (32.6%, 29/89) and horses (7.9%, 7/89). Other reported livestock species included the goat (4.5%, 4/89), buffalo (2.2%, 2/89), and one case each in the donkey, deer, mule, llama and pig (all 1.1%, 1/89).

Geographical distribution and species differentiation of photosensitisation outbreaks reported in Australia

The geographical distribution of case data in Australia was further examined by state. When peer-reviewed and non peer-reviewed reports were considered together, the highest number of
Table 1. Extracted photosensitisation outbreak data from the peer-reviewed literature by aetiological agent. Percentage morbidity and mortality are included where reported.

| Aetiological agent | Country | Type of photosensitisation | Year | Species | Flock/Herd size | Morbidity (%) | Mortality (%) | Reference |
|--------------------|---------|-----------------------------|------|---------|----------------|---------------|---------------|-----------|
| Alfalfa hay (predominantly *Medicago sativa*) | US | Primary | 2013 | Horse | 116 | 6.9 | N/A | [34] |
| Alfalfa hay (predominantly *M. sativa*) | US | Primary | 2004 | Horse | 70 | 100.0 | 1.4 | [34] |
| Alfalfa hay (predominantly *M. sativa*) | US | Primary | 2008 | Horse | N/A | N/A | N/A | [34] |
| *Alternanthera philoxeroides* (Alligator weed) | AU | Hepatogenous | 1998 | Cattle | 70 | 82.9 | N/A | [35] |
| *Anemone majus* (Bishop's weed) | US | Primary | 1978 | Sheep | N/A | N/A | N/A | [36] |
| *Biserrula pelecinus* var. Casbah and Mauro (Biserrula) | AU | Hepatogenous | 1998 | Cattle | 70 | 82.9 | N/A | [37] |
| *B. pelecinus* cv Casbah | AU | Primary | 2013 | Sheep | 120 | 25.0 | N/A | [38] |
| *B. brizantha* (Signal grass) | BR | Hepatogenous | 2013 | Sheep | 34 | 38.9 | N/A | [39] |
| *B. decumbens* (Signal grass) | BR | Primary | 2015 | Buffalo | 17 | 52.9 | N/A | [40] |
| *B. decumbens* (Signal grass) | BR | Primary | 2011 | Sheep | 80 | 16.3 | 12.5 | [41] |
| *B. decumbens* (Signal grass) | BR | Hepatogenous | 2003 | Goat | 130 | 28.3 | N/A | [42] |
| *B. decumbens* (Signal grass) | BR | Primary | 2014 | Sheep | 120 | 25.0 | 21.4 | [43] |
| *Brassica rapa* (Turnip) | NZ | Hepatogenous | 2014 | Cattle | 62 | 22.6 | 3.2 | [44] |
| *Copper* | BR | Hepatogenous | 1997 | Buffalo | 4 | 100.0 | N/A | [45] |
| *Dicrocoelium dendriticum* | UK | Hepatogenous | 2011 | Sheep | 62 | 49.2 | 3.1 | [46] |
| *Enterolobium contortisiliquum* (Pacara earpod tree) | BR | Hepatogenous | 2014 | Cattle | 62 | 22.6 | 3.2 | [47] |
| *E. contortisiliquum* (Pacara earpod tree) | BR | Primary | 2002 | Buffalo | 4 | 100.0 | N/A | [48] |
| *Flood damaged alfalfa hay* (predominantly *Medicago sativa*) | US | Hepatogenous | 1957 | Cattle | 40 | 4.2 | N/A | [49] |
| *Foxtail-or- chardgrass mixture cut hay* | US | Hepatogenous | 1991 | Cattle | 8 | 100.0 | 12.5 | [50] |
| *Froelichia humboldtiana* (Ervâncio) | BR | Primary | 2014 | Donkey | N/A | N/A | N/A | [51] |
| *F. humboldtiana* (Ervâncio) | BR | Primary | 2014 | Goat | 15 | 100.0 | N/A | [52] |
| *F. humboldtiana* (Ervâncio) | BR | Primary | 2014 | Mule | N/A | N/A | N/A | [53] |
| *F. humboldtiana* (Ervâncio) | BR | Primary | 2006 | Sheep | 5 | 100.0 | N/A | [54] |
| *F. humboldtiana* (Ervâncio) | BR | Primary | 2014 | Horse | N/A | N/A | N/A | [55] |
| *Heliotropium europaeum* (Common heliotrope) | AU | Hepatogenous | 1985 | Sheep | 120 | 7.5 | N/A | [56] |
| *Heracleum sphondylium* (Hogweed) | UK | Primary | 2010 | Horse | N/A | N/A | N/A | [57] |
| *Hypericum erectum* (St. John’s wort) | JP | Primary | 1980 | Cattle | 5 | 100.0 | N/A | [58] |
| *H. erectum* (St. John’s wort) | TN | Primary | 1999 | Horse | 34 | N/A | N/A | [59] |
| *Jamesdicksonia dactylidis* | AU | Hepatogenous | 2017 | Cattle | 678 | 24.3 | 2.8 | [60] |
| *Liver fluke* | AT | Hepatogenous | 2003 | Cattle | 120 | 7.5 | N/A | [61] |
| *Lotus corniculatus* (Birdsfoot trefoil) | NZ | Primary | 1992 | Sheep | 50 | 7.5 | N/A | [62] |
| *L. corniculatus* (Birdsfoot trefoil) | NZ | Primary | 1993 | Sheep | 56 | 26.8 | N/A | [63] |
| *Malachra fasciata* (Malachra) | BR | Primary | 2016 | Sheep | 3 | 100.0 | N/A | [64] |
| *Medicago sativa* (Lucerne, alfalfa) | ES | Primary | 2004 | Sheep | 1850 | 24.3 | N/A | [65] |
| *Microcystis aeruginosa* | SA | Hepatogenous | 1993 | Cattle | N/A | N/A | N/A | [66] |
| *Myoporum insulare* (Common boobialla) | AU | Hepatogenous | 1980 | Cattle | 177 | 14.1 | 6.2 | [67] |

(Continued)
Table 1. (Continued)

| Aetiological agent                          | Country | Type of photosensitisation | Year  | Species | Flock/Herd size | Morbidity (%) | Mortality (%) | Reference |
|--------------------------------------------|---------|-----------------------------|-------|---------|-----------------|---------------|---------------|-----------|
| Narthecium ossifragum (Bog asphodel)       | NO      | Hepatogenous                | 1999  | Sheep   | 165             | 9.7           | N/A           | [66]      |
| N. ossifragum (Bog asphodel)               | NO      | Hepatogenous                | 1990  | Sheep   | 28              | 17.9          | N/A           | [18]      |
| Nodularia spumigena                        | SA      | Hepatogenous                | 1993  | Cattle  | N/A             | N/A           | N/A           | [64]      |
| N. spumigena                               | SA      | Hepatogenous                | 1993  | Sheep   | N/A             | N/A           | N/A           | [64]      |
| Pangola grass                              | TW      | Hepatogenous                | 1978  | Cattle  | 8428            | 4.9           | 1.4           | [67]      |
| Panicum coloratum (Klein grass)            | US      | Hepatogenous                | 1987  | Sheep   | 24              | 100.0         | N/A           | [68]      |
| P. coloratum (Klein grass)                 | AU      | Hepatogenous                | 1989  | Sheep   | 2000            | N/A           | N/A           | [69]      |
| Panicum dichotomiflorum (Fall panicum)     | BR      | Hepatogenous                | 2009  | Sheep   | 365             | 22.2          | 10.7          | [70]      |
| P. dichotomiflorum (Fall panicum)          | US      | Hepatogenous                | 2006  | Horse   | 14              | 100.0         | 35.7          | [71]      |
| Panicum miliaceum (Proso millet)           | IR      | Hepatogenous                | 2008  | Sheep   | 10              | 10.0          | N/A           | [72]      |
| P. miliaceum (Proso millet)                | IR      | Hepatogenous                | 2008  | Sheep   | 253             | 32.8          | 16.2          | [73]      |
| Panicum schinzii (Sweet grass)             | AU      | Hepatogenous                | 1986  | Sheep   | 200             | 30.0          | 20.0          | [74]      |
| P. schinzii (Sweet grass)                  | AU      | Hepatogenous                | 1986  | Sheep   | 200             | 28.6          | 21.4          | [75]      |
| P. schinzii (Sweet grass)                  | AU      | Hepatogenous                | 1986  | Sheep   | 200             | 25.0          | 15.0          | [74]      |
| Panicum virgatum (Switch grass)            | US      | Hepatogenous                | 1991  | Sheep   | 104             | 16.4          | N/A           | [76]      |
| Persicaria lapathifolia (Pale knotweed)    | AU      | Hepatogenous                | 2009  | Cattle  | 50              | 4.0           | 20.0          | [15]      |
| Persicaria lapathifolia and P. orientalis  | AU      | Hepatogenous                | 2009  | Cattle  | 50              | 4.0           | 20.0          | [15]      |
| Phytolacca octandra (Inkweed)              | NZ      | Hepatogenous                | 2006  | Cattle  | 400             | 5.0           | N/A           | [78]      |
| Pityomyces chartarum                       | NZ      | Hepatogenous                | 1997  | Fallow deer | 20            | 60.0          | 30.0          | [79]      |
| P. chartarum                               | AU      | Hepatogenous                | 1985  | Sheep   | 200             | 15.0          | N/A           | [80]      |
| P. chartarum                               | SA      | Hepatogenous                | 1970  | Sheep   | N/A             | N/A           | N/A           | [81]      |
| P. chartarum                               | TR      | Hepatogenous                | 2005  | Sheep   | 1000            | 2.2           | N/A           | [82]      |
| P. chartarum                               | US      | Hepatogenous                | 1994  | Sheep   | N/A             | N/A           | N/A           | [83]      |
| P. chartarum                               | AU      | Hepatogenous                | 1978  | Sheep   | 22698           | 10.7          | 4.1           | [84]      |
| Polygonum lapathifolium (Pale persicaria)  | AU      | Hepatogenous                | 1986  | Cattle  | 380             | N/A           | 1.6           | [85]      |
| Porphyris                                  | UK      | CEP                         | 2008  | Cattle  | N/A             | N/A           | N/A           | [86]      |
| Porphyris                                  | UK      | CEP                         | 1956  | Cattle  | N/A             | N/A           | N/A           | [87]      |
| Protoporphyrin                             | FR      | CEPP                        | 1991  | Cattle  | N/A             | N/A           | N/A           | [88]      |
| Protoporphyrin                             | IE      | CEPP                        | 2015  | Cattle  | 20              | 5.0           | N/A           | [89]      |
| Protoporphyrin                             | NZ      | CEPP                        | 2011  | Cattle  | N/A             | N/A           | N/A           | [90]      |
| Protoporphyrin                             | UK      | CEPP                        | 2000  | Cattle  | 20              | 5.0           | N/A           | [91]      |
| Protoporphyrin                             | UK      | CEPP                        | 2013  | Cattle  | 26              | 7.7           | N/A           | [92]      |
| Protoporphyrin                             | US      | CEPP                        | 1999  | Cattle  | 70              | 1.4           | N/A           | [93]      |
| Senecio brasiliensis (Flor-das-almas)      | BR      | Hepatogenous                | 2013  | Cattle  | 162             | 51.2          | N/A           | [94]      |
| Senecio spp                                | BR      | Hepatogenous                | 2014  | Sheep   | 860             | 0.9           | 1.2           | [95]      |
| Tribulus terrestris (Goat's-head, puncture vine) | AU | Hepatogenous | 1983  | Goat    | 35              | 17.1          | 5.7           | [96]      |
| T. terrestris (Goat's-head, puncture vine) | AU      | Hepatogenous                | 1982  | Sheep   | 1200            | 20.8          | 14.7          | [11]      |
| T. terrestris (Goat's-head, puncture vine) | IR      | Hepatogenous                | 1998  | Sheep   | 11              | 100.0         | N/A           | [22]      |
| T. terrestris (Goat's-head, puncture vine) | IR      | Hepatogenous                | 1975  | Sheep   | 700             | 8.5           | 4.3           | [97]      |
| T. terrestris (Goat's-head, puncture vine) | TR      | Hepatogenous                | 2013  | Sheep   | 24              | 100.0         | N/A           | [98]      |
| T. terrestris (Goat's-head, puncture vine) | AU      | Hepatogenous                | 1982  | Sheep   | 190             | 36.8          | 24.2          | [11]      |
| Trifolium alexandrinum (Berseem)           | IN      | Hepatogenous                | 2013  | Cattle  | N/A             | N/A           | N/A           | [99]      |
| Unidentified                               | MY      | Hepatogenous                | 2012  | Cattle  | N/A             | N/A           | N/A           | [100]     |
| Unidentified                               | AU      | Hepatogenous                | 1985  | Sheep   | 35              | 42.9          | 28.6          | [74]      |
| Unidentified                               | AU      | Hepatogenous                | 1986  | Sheep   | 100             | 7.0           | N/A           | [74]      |
outbreaks was observed in New South Wales and Victoria (33 reports each), followed by Queensland (15 reports), Western Australia (15 reports), Tasmania (9 reports), and South Australia (4 reports) (Fig 3). There was no photosensitisation case report from the Northern Territory. *Panicum* spp., *P. chartarum* and *T. terrestris* were clearly represented as causal agents with 12, 4, and 4 cases reported respectively. However, *Lantana* spp. (15 reports) and *Cynosurus echinatus* (9 reports) are also prevalent within specific geographical locations (*Lantana* spp. in Queensland and *C. echinatus* in Victoria, Table 2).

As observed in global cases, a similar species predisposition, or reporting bias, was observed in reports from Australia. Sheep and cattle presented as the most frequently reported livestock species in photosensitisation outbreaks in Australia. Over 54% (40/74) of reported outbreaks concerned sheep, 43.2% (32/74) cattle, with the remaining outbreaks horse and goat (1 case only in each species).

**Prevalence of category of photosensitisation in livestock and aetiological agent, a global analysis**

In all peer-reviewed articles examined, 68.5% (61/89) reported cases were suspected or confirmed to be cases of hepatogenous (Type III) photosensitisation (Table 1). In comparison, only 22.5% (20/89) reported cases, were diagnosed or suspected to be primary (Type I) in nature. Only 9.0% (8/89) reported cases of outbreaks in the US, UK, New Zealand, Ireland, and France, were diagnosed or suspected as congenital (Type II) photosensitisation (Fig 4).

Common aetiological agents were reported in multiple locations globally (Fig 5). For example, *Brachiaria decumbens* has been reported as a causal agent in Brazil, Colombia, and Nigeria; various species of the *Panicum* genus of grasses have been identified as causal agents in outbreaks of photosensitisation in Australia, Brazil, Iran, and the United States; *P. chartarum*, a fungus that produces a specific mycotoxin called sporidesmin, was reported as an aetiological cause of hepatogenous photosensitisation in Australia, New Zealand, South Africa, Turkey, and the United States; *Tribulus terrestris* was reported as a causal species in Australia, Iran, and Turkey. Certain species were found to have a more contained geographical distribution, for example, *F. humboldtiana*, a primary photosensitising plant, was identified in six cases solely occurring in Brazil. *Biserrula* spp., an annual legume from the Mediterranean [102], was reported as a causative agent of primary photosensitisation only in Australia (Table 1, Fig 5).

Congenital cases of photosensitisation accounted for the least number of outbreaks which were restricted to the United Kingdom (4), France (1), Ireland (1), New Zealand (1), and the United States (1) (Table 1).

**Causative agents of photosensitisation in Australia**

Analysis of published photosensitisation case reports in Australia alone, taking both peer-reviewed and non peer-reviewed reports together, identified that outbreaks of

---

**Table 1.** (Continued)

| Aetiological agent | Country | Type of photosensitisation | Year | Species | Flock/Herd size | Morbidity (%) | Mortality (%) | Reference |
|-------------------|---------|---------------------------|------|---------|-----------------|---------------|--------------|-----------|
| *Unidentified* (White clover, phalaris and rye grass) | AU       | Hepatogenous               | 1964 | Sheep   | 100             | 20.0          | N/A          | [101]     |

N/A, not available; CEPP, Congenital Erythropoietic Protoporphyria; CEPP, Congenital Erythropoietic Protoporphyria; AU, Australia; AT, Austria; BR, Brazil; CO, Columbia; FR, France; IN, India; IR, Iran; IRE, Ireland; JP, Japan; MY, Malaysia; NZ, New Zealand; NG, Nigeria; NO, Norway; SA, South Africa; ES, Spain; TW, Taiwan; TN, Tunisia; TR, Turkey; UK, United Kingdom; US, United States

[101] https://doi.org/10.1371/journal.pone.0211625.t001

outbreaks was observed in New South Wales and Victoria (33 reports each), followed by Queensland (15 reports), Western Australia (15 reports), Tasmania (9 reports), and South Australia (4 reports) (Fig 3). There was no photosensitisation case report from the Northern Territory.

*Panicum* spp., *P. chartarum* and *T. terrestris* were clearly represented as causal agents with 12, 4, and 4 cases reported respectively. However, *Lantana* spp. (15 reports) and *Cynosurus echinatus* (9 reports) are also prevalent within specific geographical locations (*Lantana* spp. in Queensland and *C. echinatus* in Victoria, Table 2).

As observed in global cases, a similar species predisposition, or reporting bias, was observed in reports from Australia. Sheep and cattle presented as the most frequently reported livestock species in photosensitisation outbreaks in Australia. Over 54% (40/74) of reported outbreaks concerned sheep, 43.2% (32/74) cattle, with the remaining outbreaks horse and goat (1 case only in each species).

**Prevalence of category of photosensitisation in livestock and aetiological agent, a global analysis**

In all peer-reviewed articles examined, 68.5% (61/89) reported cases were suspected or confirmed to be cases of hepatogenous (Type III) photosensitisation (Table 1). In comparison, only 22.5% (20/89) reported cases, were diagnosed or suspected to be primary (Type I) in nature. Only 9.0% (8/89) reported cases of outbreaks in the US, UK, New Zealand, Ireland, and France, were diagnosed or suspected as congenital (Type II) photosensitisation (Fig 4).

Common aetiological agents were reported in multiple locations globally (Fig 5). For example, *Brachiaria decumbens* has been reported as a causal agent in Brazil, Colombia, and Nigeria; various species of the *Panicum* genus of grasses have been identified as causal agents in outbreaks of photosensitisation in Australia, Brazil, Iran, and the United States; *P. chartarum*, a fungus that produces a specific mycotoxin called sporidesmin, was reported as an aetiological cause of hepatogenous photosensitisation in Australia, New Zealand, South Africa, Turkey, and the United States; *Tribulus terrestris* was reported as a causal species in Australia, Iran, and Turkey. Certain species were found to have a more contained geographical distribution, for example, *F. humboldtiana*, a primary photosensitising plant, was identified in six cases solely occurring in Brazil. *Biserrula* spp., an annual legume from the Mediterranean [102], was reported as a causative agent of primary photosensitisation only in Australia (Table 1, Fig 5).

Congenital cases of photosensitisation accounted for the least number of outbreaks which were restricted to the United Kingdom (4), France (1), Ireland (1), New Zealand (1), and the United States (1) (Table 1).

**Causative agents of photosensitisation in Australia**

Analysis of published photosensitisation case reports in Australia alone, taking both peer-reviewed and non peer-reviewed reports together, identified that outbreaks of
Table 2. Photosensitisation outbreaks in livestock in Australia extracted from two non peer-reviewed publication series. Percentage morbidity and mortality are included where available.

| Aetiological agent | State | Type   | Species          | Flock/Herd size | Morbidity (%) | Mortality (%) | Reference         |
|---------------------|-------|--------|------------------|-----------------|---------------|---------------|-------------------|
| **B. decumbens** (Signal grass) | WA    | Hepatogenous | Sheep | 300 | 20.0 | N/A | AHSQR 17: 1 |
| **Biserrula casbah** (Biserrula) | WA    | Primary | Sheep | 500 | 40.0 | N/A | AHSQR 7: 3 |
| **Biserrula or clover** | WA    | Primary | Sheep | N/A | N/A | N/A | AHSQR 9: 4 |
| **Biserrula spp.** (Biserrula) | WA    | Primary | Cattle | N/A | N/A | N/A | AHSQR 16: 2 |
| **Brassica napus** (Rape, canola) | VIC   | Hepatogenous | Cattle | 200 | 3.0 | N/A | AHSQR 14: 1 |
| **Brassica spp.** | VIC   | Hepatogenous | Cattle | N/A | N/A | N/A | AHSQR 4: 1 |
| Cynosurus echinatus (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 9 | N/A | 22.2 | AHSQR 19: 2 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 25 | 24.0 | N/A | AHSQR 11: 2 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 35 | 28.6 | N/A | AHSQR 11: 2 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | N/A | N/A | N/A | AHSQR 6: 2 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 510 | 32.4 | 10.0 | AHSQR 7: 2 |
| **C. echinatus** (Rough dog’s tail grass) | WA    | Hepatogenous | Cattle | N/A | N/A | N/A | AHSQR 7: 3 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 270 | 11.9 | 0.7 | AHSQR 8: 2 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 11 | 100.0 | N/A | AHSQR 15: 2 |
| **C. echinatus** (Rough dog’s tail grass) | VIC   | Hepatogenous | Cattle | 150 | 53.3 | N/A | AHSQR 18: 2 |
| **Echinochloa utilis** (Japanese barnyard millet) | VIC   | Hepatogenous | Sheep | 300 | 10.0 | 6.7 | AHSQR 14: 4 |
| **Heliotrope spp.** | VIC   | Hepatogenous | Sheep | N/A | N/A | N/A | AHSQR 6: 3 |
| Heliotropium europaeum (Common heliotrope) | NSW   | Hepatogenous | Cattle | 60 | 100.0 | 66.7 | F&H Sep, 2015 |
| **H. europaeum** (Common heliotrope) | NSW   | Hepatogenous | Sheep | N/A | N/A | N/A | AHSQR 19: 4 |
| Hypericum perforatum (St John’s wort) | NSW   | Primary | Sheep | 550 | 33.6 | N/A | F&H Mar, 2012 |
| **H. perforatum** (St John’s wort) | NSW   | Primary | Sheep | 300 | 50.0 | 3.3 | AHSQR 13: 4 |
| **Lantana camara** (Lantana) | QLD   | Hepatogenous | Cattle | 100 | N/A | 3.0 | AHSQR 11: 1 |
| **L. camara** (Lantana) | QLD   | Hepatogenous | Cattle | 35 | 5.7 | 2.8 | AHSQR 12: 1 |
| **L. camara** (Lantana) | NSW   | Hepatogenous | Cattle | N/A | N/A | N/A | AHSQR 14: 3 |
| **L. camara** (Lantana) | QLD   | Hepatogenous | Cattle | 250 | N/A | 3.2 | AHSQR 16: 3 |
| **L. camara** (Lantana) | QLD   | Hepatogenous | Cattle | 250 | 0.8 | N/A | AHSQR 16: 3 |
| **L. camara** (Lantana) | QLD   | Hepatogenous | Cattle | 20 | 50.0 | N/A | AHSQR 16: 3 |
| **L. camara** (Lantana) | QLD   | Hepatogenous | Cattle | 80 | N/A | 7.5 | AHSQR 21: 1 |
| **L. camara** (Lantana) | NSW   | Hepatogenous | Cattle | 47 | N/A | 19.2 | AHSQR 8: 1 |
| **L. camara** (Lantana) | QLD   | Hepatogenous | Cattle | 120 | N/A | 2.5 | AHSQR 10: 2 |

(Continued)
| Aetiological agent     | State | Type       | Species | Flock/Herd size | Morbidity (%) | Mortality (%) | Reference          |
|------------------------|-------|------------|---------|----------------|---------------|---------------|--------------------|
| Lantana spp.           | NSW   | Hepatogenous | Cattle  | 47             | N/A           | N/A           | AHSQR 11:4         |
| Lantana spp.           | QLD   | Hepatogenous | Cattle  | N/A            | N/A           | N/A           | AHSQR 12:4         |
| Lantana spp.           | QLD   | Hepatogenous | Cattle  | 220            | 5.9           | 1.4           | AHSQR 4:2          |
| Lantana spp.           | QLD   | Hepatogenous | Cattle  | 800            | 18.8          | N/A           | AHSQR 7:2          |
| Lantana spp.           | QLD   | Hepatogenous | Cattle  | N/A            | N/A           | N/A           | AHSQR 7:3          |
| Lantana spp.           | QLD   | Hepatogenous | Cattle  | N/A            | N/A           | N/A           | AHSQR 9:2          |
| Lolium perenne         | VIC   | Primary     | Cattle  | 120            | 25.0          | N/A           | AHSQR 12:2         |
| Mentha pulegium        | TAS   | Primary     | Sheep   | N/A            | N/A           | N/A           | AHSQR 12:1         |
| P. chartarum           | VIC   | Hepatogenous | Cattle  | N/A            | 50.0          | 'significant' | AHSQR 4:2          |
| P. chartarum           | SA    | Hepatogenous | Cattle  | N/A            | N/A           | N/A           | AHSQR 5:2          |
| P. chartarum           | TAS   | Hepatogenous | Sheep   | N/A            | N/A           | N/A           | AHSQR 20:2         |
| P. chartarum           | VIC   | Hepatogenous | Sheep & | 114            | 5–50          | 1–30          | AHSQR 16:2         |
| P. chartarum           | WA    | Hepatogenous | Sheep   | N/A            | N/A           | N/A           | AHSQR 9:4          |
| P. chartarum           | NSW   | Hepatogenous | Sheep   | 1000           | N/A           | N/A           | F&H Dec, 2011      |
| P. chartarum           | VIC   | Hepatogenous | Cattle  | N/A            | 69.6          | 30.4          | AHSQR 6:1          |
| P. chartarum           | WA    | Hepatogenous | Cattle  | 750            | 40.0          | N/A           | AHSQR 8:2          |
| P. chartarum           | NSW   | Hepatogenous | Cattle  | 10             | 70.0          | N/A           | F&H Nov, 2015      |
| P. chartarum           | VIC   | Hepatogenous | Cattle  | N/A            | 5.1           | N/A           | F&H Sep, 2015      |
| P. chartarum           | NSW   | Hepatogenous | Sheep   | 520            | 7.7           | 1.2           | F&H Jul, 2013      |
| P. chartarum           | TAS   | Hepatogenous | Sheep   | 48             | 4.2           | N/A           | F&H Dec, 2011      |
| P. chartarum           | VIC   | Hepatogenous | Sheep   | 230            | 100.0         | N/A           | AHSQR 14:1         |
| P. effusum             | VIC   | Hepatogenous | Sheep   | 48             | 4.2           | N/A           | AHSQR 14:1         |
| P. effusum             | VIC   | Hepatogenous | Sheep   | 500            | 8.4           | N/A           | AHSQR 18:1         |
| P. coloratum           | NSW   | Hepatogenous | Sheep   | N/A            | N/A           | N/A           | AHSQR 13:1         |
| Panicum effusum        | VIC   | Hepatogenous | Sheep   | 350            | 14.3          | 8.6           | AHSQR 15:1         |
| Panicum gilvum         | NSW   | Hepatogenous | Sheep   | 520            | 7.7           | 1.2           | AHSQR 15:1         |
| Panicum hillmanii      | VIC   | Hepatogenous | Sheep   | 400            | 6.3           | N/A           | AHSQR 14:1         |
| Panicum miliaceum      | WA    | Hepatogenous | Sheep   | N/A            | N/A           | N/A           | AHSQR 11:3         |
| Panicum spp.           | NSW   | Hepatogenous | Sheep   | many           | N/A           | N/A           | F&H, 1981          |
| Panicum spp.           | NSW   | Hepatogenous | Sheep   | N/A            | 10            | N/A           | AHSQR 1:2          |
| Panicum spp.           | VIC   | Hepatogenous | Sheep   | 2170           | N/A           | 1.4           | AHSQR 20:1         |
| Panicum spp.           | VIC   | Hepatogenous | Sheep   | 200            | N/A           | 10.0          | AHSQR 9:1          |
| Panicum spp.           | NSW   | Hepatogenous | Sheep   | 450            | 5.1           | N/A           | F&H Sep, 2015      |
| Panicum spp.           | VIC   | Hepatogenous | Cattle  | 500            | 2.0           | N/A           | AHSQR 15:1         |

(Continued)
| Aetiological agent                  | State  | Type          | Species | Flock/Herd size | Morbidity (%) | Mortality (%) | Reference   |
|------------------------------------|--------|---------------|---------|-----------------|---------------|---------------|-------------|
| *Pithomyces chartarum*             | TAS    | Hepatogenous  | Cattle  | 290             | 20.7          | 0.3           | AHSQR 11:1  |
| *Pithomyces* spp.                  | NSW    | Hepatogenous  | Sheep   | 14              | 14.3          | N/A           | AHSQR 16:4  |
| *Pithomyces* spp.                  | WA     | Hepatogenous  | Sheep   | 1000            | 5.0           | N/A           | AHSQR 18:2  |
| *Polygonum* sp.                    | NSW    | Primary       | Cattle  | 130             | 3.9           | N/A           | AHSQR 14:4  |
| *T. terrestris* (Goat’s-head, puncture vine) | WA    | Hepatogenous  | Sheep   | N/A             | N/A           | N/A           | AHSQR 13:1  |
| *T. terrestris* (Goat’s-head, puncture vine) | WA    | Hepatogenous  | Sheep   | N/A             | N/A           | N/A           | AHSQR 16:3  |
| *T. terrestris* (Goat’s-head, puncture vine) | SA    | Hepatogenous  | Sheep   | 100             | N/A           | N/A           | AHSQR 9:1   |
| *Tribulus terrestris*              | NSW    | Hepatogenous  | Sheep   | N/A             | N/A           | N/A           | AHSQR 13:1  |
| *Trifolium resupinatum* (Shaftal clover) | NSW   | Hepatogenous  | Sheep   | N/A             | N/A           | N/A           | F&H 1987    |
| Unidentified                       | TAS    | Primary       | Cattle  | 150             | 3.3           | N/A           | AHSQR 12:3  |
| Unidentified                       | VIC    | Hepatogenous  | Cattle  | 300             | 6.7           | N/A           | AHSQR 15:2  |
| Unidentified                       | VIC    | Hepatogenous  | Cattle  | 250             | 20.0          | N/A           | AHSQR 15:2  |
| Unidentified                       | SA     | Hepatogenous  | Cattle  | 350             | 25.1          | 5.1           | AHSQR 15:2  |
| Unidentified                       | VIC    | Primary       | Cattle  | N/A             | N/A           | N/A           | AHSQR 15:3  |
| Unidentified                       | TAS    | Hepatogenous  | Cattle  | 100             | 13.0          | 3.0           | AHSQR 19:4  |
| Unidentified                       | TAS    | Hepatogenous  | Cattle  | 900             | 25.0          | 0.7           | AHSQR 19:4  |
| Unidentified                       | TAS    | Hepatogenous  | Cattle  | 160             | 18.8          | N/A           | AHSQR 4:2   |
| Unidentified                       | WA     | Primary       | Sheep   | N/A             | N/A           | N/A           | AHSQR 16:3  |
| Unidentified                       | NSW    | Primary       | Sheep   | N/A             | 50–100        | N/A           | AHSQR 20:2  |
| Unidentified                       | NSW    | Primary       | Sheep   | 8 flocks        | 50–100        | 5–15          | F&H Nov, 2015 |
| Unidentified (Aphid-infested thistles) | NSW    | Hepatogenous  | Cattle  | 36              | 100.0         | 41.7          | F&H 1956    |
| Unidentified (Aphids)              | WA     | Primary       | Sheep   | 4200            | N/A           | N/A           | AHSQR 12:3  |
| Unidentified (Pyrrolizidine alkaloids) | QLD  | Hepatogenous  | Horse   | 20              | 100.0         | 65.0          | AHSQR 15:2  |
| Unidentified (Pyrrolizidine alkaloids) | SA    | Hepatogenous  | Sheep   | N/A             | N/A           | N/A           | AHSQR 13:3  |
| Unidentified (Ryegrass, silage, oats, straw, grape Marc and pasture hay) | VIC  | Hepatogenous  | Cattle  | 270             | 3.7           | N/A           | AHSQR 13:1  |
| Unidentified (Ryegrass)            | VIC    | Hepatogenous  | Cattle  | 160             | 6.3           | 1.3           | AHSQR 12:2  |

N/A, not available; F&H, Flock and Herd, AHSQR, Animal Health Surveillance Quarterly; NSW, New South Wales; SA, Southern Australia; QLD, Queensland; TAS, Tasmania; VIC, Victoria; WA, Western Australia

https://doi.org/10.1371/journal.pone.0211625.t002
photosensitisation in livestock related to ingestion of the Panicum genus of grasses were the most commonly reported aetiology in this region (18/94, 19.1%, Fig 6). The second most common confirmed aetiological agent was Lantana spp. (15/94, 16.0%). The soil-borne ubiquitous fungus P. chartarum also accounted for a significant proportion of analysed case reports (14/94, 14.9%). These three agents represented the confirmed aetiological causes of the majority of photosensitisation cases reported in Australia (47/94, 50%).

**Livestock morbidity related to photosensitisation type**

Calculation of the morbidity (affected / flock number) and mortality (deaths / flock number) was compared between peer-reviewed reports (78 reports in total, Table 1) or non-peer reviewed reports (88 reports in total, Table 2) where the aetiological agent had been specified. The extracted data was visualised using a violin plot (Fig 7). This analysis showed a wide variation in morbidity and mortality between the two publication modalities with the peer reviewed publications showing higher figures for morbidity than those in non-peer reviewed publications. No photosensitisation related deaths were in outbreaks of congenital photosensitisation, and analysis showed that hepatogenous photosensitisation exhibited wider variation in morbidity and mortality than outbreaks of primary photosensitisation (Fig 7). Specifically, of the
26 peer-reviewed reports that described mortality related to photosensitisation, 25 were hepatogenous in nature. Only one mortality was associated with an outbreak of primary photosensitisation whilst none were associated with congenital cases (Fig 7a). Morbidity varied greatly ranging from 5–100% (Fig 7b).

Discussion

Photosensitisation outbreaks are commonly reported in Australasia, Brazil and the United States

Reporting bias was implicit in the method used for report extraction and data compilation in this study as only reports with a full text or abstract in English were selected for review and this fact explains, in part, the high numbers of case reports identified in Australia and the United States specifically. Each of these countries has a strong track record in scientific publication in the veterinary field, produces large numbers of sheep and cattle, also the most frequently reported livestock species in photosensitisation outbreaks (Table 1, Fig 2), and relies significantly on livestock production for export.

The number of reported cases from Europe as a whole was relatively low with only 12 articles found in the literature for this region. This finding suggests that photosensitisation is less of an issue for European farming systems compared to those of Australia, New Zealand, Brazil, and the US. Differences in climate [13–17], farming practices [12], availability of non-toxic pasture species and native or invasive weed species [103,104] associated with primary or secondary photosensitisation are likely to be playing a key role in this finding. However, the study selection criteria also would have been biased for publications from a large number of European countries as well. It possible that some photosensitisation outbreaks have been...
reported in native language publications, which would not have been selected due to the filtering process. Nevertheless, the large number of case reports published in Brazil, identifying a diverse range of plant species as causally related to outbreaks of photosensitisation (Table 1, Fig 2), suggests that publication language barrier is not necessarily an obstacle to presentation of case reports in the literature, where English is the common language of scientific publication.

Hepatogenous photosensitisation is common in domestic livestock

This report identifies hepatogenous photosensitisation to be the most common presentation of clinical photosensitisation in livestock (Fig 4), a finding in agreement with the general scientific literature [2]. Although inter-species and intra-species variation in sensitivity to photosensitising agents exists, toxic plants and organisms capable of causing outbreaks in domestic livestock should also be considered a potential risk to all grazing herbivores. This is particularly the case for native wildlife where plant-related outbreaks of hepatogenous photosensitisation have been reported in kangaroos and wombats [105–107].

Congenital (Type II) photosensitisation was rarely identified in the published literature (8/89 reports) in this study. Congenital erythropoietic protoporphyria has only been reported in
cattle, and only in a small number of countries in Europe as well as the United States and New Zealand. This likely reflects the common ancestry of many cattle herds in aforementioned two countries with animals largely exported to these regions from the United Kingdom, and therefore the reliance on a small genetic pool of beef cattle in particular [90,93]. Interestingly, despite presenting with the highest number of peer-reviewed case reports, no congenital photosensitisation cases have yet been reported in Australia. This is likely a reflection of the selectivity of Australian livestock import systems and reliance on a highly conserved gene pool present in the cattle imported into this jurisdiction.

Photosensitisation shows highly variable morbidity and mortality worldwide

A high degree of variability was reported for both morbidity and mortality in outbreaks of both primary and hepatogenous photosensitisation (Tables 1 & 2, Fig 7). This further suggests the difficulty of attributing an overall economic impact of photosensitisation to the global livestock industry, since the severity and magnitude of each outbreak is multifactorial and can differ significantly. An additional confounding factor is that higher mortality rates were recorded in hepatogenous photosensitisation found in peer-reviewed case reports compared to those

![Diagram of causative agents identified in peer-reviewed photosensitisation case reports worldwide.](https://doi.org/10.1371/journal.pone.0211625.g005)
reported in non-peer reviewed publications (Fig 7a), suggesting that only the most severe photosensitisation outbreaks were selected to be published by attending clinicians. This supports the author’s anecdotal findings that the majority of photosensitisation outbreaks are either submitted for publication in non peer-reviewed publications, or are not reported in print at all.

**Prevalence of photosensitisation case reports in Australia**

Outbreak reports in this analysis represent a bias towards Australia. Certain countries, such as New Zealand, are also known anecdotally to have a high incidence of photosensitisation. The incidence of New Zealand may be underrepresented in this review as the available reporting systems for these outbreaks are not as apparent as Australia, where there is a strong network of government veterinarians and good mechanisms for the presentation of non peer-reviewed case reports. It is also widely acknowledged that the more common a disease, the less a producer is likely to request the services of a veterinarian for diagnoses, and the less a veterinarian is likely to report the outbreak formally.

Australia has experienced outbreaks of primary photosensitisation that are specific and unique to this region. One example is photosensitisation caused by the pasture legume...
Biserrula pelecinus, although a native of the southern Mediterranean, it is exclusively used as a livestock fodder only in Australia [102] where this pasture legume is now clearly identified as causing outbreaks of primary photosensitisation [37,38]. Outbreaks that have never been recorded in its native domains where it grows as a native only in mixed swards. The specific need to identify drought tolerant, hardy annuals to fill the summer feed gap in Australian livestock production systems therefore resulted in introduction of pasture species that has selectively caused livestock toxicity [108]. This situation is not unique to Australia but this is the first clearly correlated example of an introduced species being propagated for pasture fodder which then gives rise to consistent outbreaks of primary photosensitisation in production livestock.

The majority of reports of photosensitisation cases in Australia reported in this review were located were in two states: New South Wales and Victoria (Fig 3). The disproportionate representation of these two states in this dataset is a reflection of a) the relatively high number of primary beef and lamb producers operating in these two states in Australia, and b) reporting bias due to availability of non-peer reviewed case reports presented in producer publications such as ‘Flock and Herd’ (a NSW publication). However, this relative over-reporting in our view does not rule out our findings that under-reporting of clinical outbreaks is still occurring in Australia due to the perception that photosensitisation is ‘common’ in production flocks and herds (Y. Chen, survey of Australian veterinarians, unpublished data). Both states also showed a higher prevalence of causes related to Panicum genus of grasses and P. chartarum. Outbreaks in Queensland, by comparison, were mainly related to ingestion of the toxic weed species
Lantana spp. These different causal species profiles suggest that environmental adaptation of such invasive plants is critical to their establishment and therefore the prevalence of toxicity associated with them [12,109].

An interesting finding that emerged from analysis of the non peer-reviewed Australian literature in this study was the identification of *C. echinatus* (rough dog's tail) as a putative causative agent in outbreaks of hepatogenous photosensitisation from eight separate reports in Victoria and Western Australia (Table 2). Despite its common appearance in the non peer-reviewed literature, this plant has not been formally confirmed to be associated with an outbreak of photosensitisation [110] where controlled feeding trials have been unable to confirm *C. echinatus* as causing hepatotoxic damage sufficient to cause secondary clinical photosensitivity [111]. This contradictory evidence further suggests that anecdotal case reports should be viewed cautiously until true causality has been proven, as many epidemiological investigations focus on commonalities rather than specifics in outbreak patterns. In cases of photosensitisation a causal relationship between the clinical signs and the suspected agent(s) cannot be assumed to be proven until a direct or evidence-based causation can be established.

**Objective measurement of clinical signs of photosensitisation in domestic species**

Morbidity in outbreaks of photosensitisation, of all underlying aetiological causes, was found to be highly variable in the literature. This variation is likely to be caused by reporting error by the producer or veterinarian based on inconsistent identification of affected animals. One issue that may have hampered accurate identification of the number of animals affected in outbreaks is the fact that mild cases are commonly overlooked by both the producer and veterinarian, therefore under-reporting of morbidity is likely to occur. Previously, no objective photosensitisation scoring protocol had been defined in literature resulting in prevalence and severity of affected animals to be hard to compare between outbreaks. Recently, a semi-objective photosensitisation grading system has been developed for sheep to address this issue [37]. The use of such a grading system in future outbreaks will allow better correlation between access to potentially photosensitising pastures or feedstuffs with more accurate determination of the timing of onset of outbreaks, as well as a more definitive and consistent identification of the severity of the condition. Furthermore, a mechanism for *de novo* case reporting related to known causal agents, not just those that are novel or unusual, (such as seen with the publication 'Flock and Herd' or via an incidence register) would better document the prevalence, and therefore economic impact, of photosensitisation globally.

**Conclusions**

Photosensitisation is a common, but likely underreported, entity in the literature. Hepatogenous photosensitisation is by far the most common presentation. Some species, the *Panicum* genus of grasses and *Pithomyces chartarum* in particular, consistently were reported in photosensitisation cases. Novel species are also implicated in outbreaks of photosensitisation, including pasture legumes *Biserrula pelecinus*, but primary photosensitisation is a rare occurrence in general. Significant variation in both morbidity, mortality and severity was observed in both peer-reviewed and non-peer reviewed reports. Variations in reported outbreaks may reflect true differences in morbidity rates between aetiological agents, but may also be partly due to the fact that mild presentations are overlooked, and lesions are not consistently graded by an unified standard. Together, our findings help identify the aetiology and geographical patterns, the plant and animal species implicated, and morbidity and mortality patterns of photosensitisation in livestock globally. This suggests that control of pasture species or weeds known to
cause toxic outbreaks would have a significant impact on the prevalence of the condition in livestock globally, but also particularly in Australia, Brazil, and the United States where these outbreaks appear to be more common.

Supporting information
S1 PRISMA Checklist.

Acknowledgments
The authors acknowledge financial support from the Graham Centre for Agricultural Innovation and School of Animal and Veterinary Science (Charles Sturt University). The authors would like to thank Dr. Paul Weston for consultation on the data presentation methods from the statistical perspective. The authors would also like to thank Animal Health Australia (www.animalhealthaustralia.com.au) for providing access to archived reports of Animal Health Surveillance Quarterly.

Author Contributions
Conceptualization: Yuchi Chen, Jane C. Quinn, Panayiotis Loukopoulos.
Data curation: Yuchi Chen, Panayiotis Loukopoulos.
Formal analysis: Yuchi Chen, Panayiotis Loukopoulos.
Investigation: Yuchi Chen.
Methodology: Yuchi Chen, Panayiotis Loukopoulos.
Project administration: Yuchi Chen.
Supervision: Jane C. Quinn, Leslie A. Weston, Panayiotis Loukopoulos.
Validation: Yuchi Chen.
Visualization: Yuchi Chen.
Writing – original draft: Yuchi Chen, Jane C. Quinn.
Writing – review & editing: Yuchi Chen, Jane C. Quinn, Leslie A. Weston, Panayiotis Loukopoulos.

References
1. Rowe LD. Photosensitization problems in livestock. Vet Clin of Nor Am: Fo Ani Prac. 1989; 5: 301–323. https://doi.org/10.1016/S0749-0720(15)30978-6
2. Mauldin EA, Peters-Kennedy J. Integumentary System. In: Maxie MG, editor. Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. 6 ed. St. Louis; 2016. pp. 577–580.
3. Fu PP, Xia Q, Zhao Y, Wang S, Yu H, Chiang HM. Phototoxicity of herbal plants and herbal products. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2013; 31: 213–255. https://doi.org/10.1080/10590501.2013.824206 PMID: 24024520
4. Quinn JC, Kessell A, Weston LA. Secondary plant products causing photosensitization in grazing herbivores: Their structure, activity and regulation. Int J Mol Sci. 2014; 15: 1441–1465. https://doi.org/10.3390/ijms15011441 PMID: 24451131
5. Barrington GM. Integumentary System. In: Kahn CM, editor. The Merck Veterinary Manual. 10 ed. London, United Kingdom: Wiley; 2010. pp. 665–800.
6. Doyle KA, Gordon H. Merck Veterinary Manual. Blackwell Publishing Ltd; 2008. pp. 278–278. https://doi.org/10.1111/j.1751-0813.1993.tb08058.x
7. Kellerman TS, Coetzer JA. Hepatogenous photosensitivity diseases in South Africa. Onderstepoort J Vet Res. 1985; 52: 157–173. PMID: 3911131
8. Flåøyen A. Plant-associated hepatogenous photosensitization diseases. In: Tu AT, Gaffield W, editors. Natural and Selected Synthetic Toxins. 1999. pp. 204–219.
9. McKenzie R. Australia’s Poisonous Plants, Fungi and Cyanobacteria. CSIRO Publishing; 2012. https://doi.org/10.1111/j.1751-0813.2012.01001.x
10. Kingsbury JM. Plants poisonous to livestock. A review. J Dairy Sci. 1958; 41: 875–907. https://doi.org/10.3168/jds.S0022-0302(58)91020-8
11. Glastonbury JRW, Doughty FR, Whitaker SJ, Sergant E. A syndrome of hepatogenous photosensitisation, resembling geeldikkop, in sheep grazing Tribulus terrestris. Aust Vet J. 1984; 61: 314–316. https://doi.org/10.1111/avj.12148 PMID: 6525116
12. Pollock ML, Wishart H, Holland JP, Malone FE, Waterhouse A. Photosensitisation of livestock grazing Narthecium ossifragum: Current knowledge and future directions. Vet J. 2015; 206: 275–283. https://doi.org/10.1016/j.tvjl.2015.07.022 PMID: 26324639
13. Peterson JE, Payne A, Culvenor CC. Heliotropium europaeum poisoning of sheep with low liver copper concentrations and the preventive efficacy of cobalt and antimethanogen. Aust Vet J. 1992; 69: 51–56. PMID: 1316747
14. Aslani MR, Movassaghi AR, Mohri M, Pedram M, Abavasi A. Experimental Tribulus terrestris poisoning in sheep: Clinical, laboratory and pathological findings. Vet Res Commun. 2003; 27: 53–62. https://doi.org/10.1023/A:1022010707704
15. Medeiros RMT, Bezerra VKD, Riet-Correa F. Experimental poisoning by Brachiaria decumbens in feedlot sheep. Pesq Vet Bras. 2010; 30: 195–202. https://doi.org/10.1590/S0100-736X2010000300002
16. Di Menna ME, Flåøyen A, Ulvund MJ. Fungi on Narthecium ossifragum leaves and their possible involvement in alveld disease of Norwegian lambs. Vet Res Commun. 1992; 16: 117–124. PMID: 1496813
17. Sandler IL. Photosensitizing agents: a brief review of the literature. J Am Med Assoc. American Medical Association; 1939; 112: 2411–2413. https://doi.org/10.1001/jama.1939.628002300002012b
18. Barnes J, Anderson LA, Phillipson JD. St John’s wort (Hypericum perforatum L.): A review of its chemistry, pharmacology and clinical properties. Journal of Pharmacy and Pharmacology. Blackwell Publishing Ltd; 2001; 53: 583–600. https://doi.org/10.1211/0022357011775910
31. Hussain SM, Herling VR, Rodrigues PHM, Naz I, Khan H, Khan MT. Mini review on photosensitization by plants in grazing herbivores. Trop Anim Health Prod. 2018; 36: 1–11. https://doi.org/10.1007/s11250-018-1583-x PMID: 29623517

32. Laustriat G. Molecular mechanisms of photosensitization. Biochimie. 1986; 68: 771–778. https://doi.org/10.1016/0300-9084(86)80092-X PMID: 3019431

33. Knupp SNR, Knupp LS, Riet-Correia F, Lucena RB. Plants that cause photosensitivity in ruminants in Brazil. Semina:Cienc Agrarias. 2016; 37: 2009–2020. https://doi.org/10.5433/1679-0359.2016v37n4p2009

34. Puschner B, Chen X, Read D, Affolter VK. Alfalfa hay induced primary photosensitization in horses. Vet J. 2016; 211: 32–38. https://doi.org/10.1016/j.tvjl.2016.03.004 PMID: 27040919

35. Bourke CA, Rayward D. Photosensitisation in dairy cattle grazing alligator weed (Alternanthera philoxeroides) infested pastures. Aust Vet J. 2003; 81: 361–362. https://doi.org/10.1111/j.1751-0813.2003.tb11515.x PMID: 15080460

36. Witzel DA, Dollahite JW, Jones LP. Photosensitization in sheep fed Ammi majus (Bishop’s weed) seed. Am J Vet Res. 1978; 39: 319–320. PMID: 564651

37. Quinn JC, Chen Y, Hackney B, Tufail MS, Weston LA, Loukopoulou P. Acute-onset high-morbidity primary photosensitisation in sheep associated with consumption of the Casbah and Mauro cultivars of the pasture legume Biserrula. BMC Vet Res. 2018; 14: 11. https://doi.org/10.1186/s12917-017-1318-7 PMID: 29325550

38. Kessell AE, Ladmorre GE, Quinn JC. An outbreak of primary photosensitisation in lambs secondary to consumption of Biserrula pelecinus (biserrula). Aust Vet J. 2015; 93: 174–178. https://doi.org/10.1111/avj.12318 PMID: 25939266

39. de Lemos RAA, Nakazato L, Herrero Junior GO, Silveira AC, Porfirio LC. Fotossensibilização e colangiopatia associada a cristais em caprinos mantidos sob pastagens de Brachiaria decumbens no Mato Grosso do Sul. Ciência Rural. 1998; 28: 507–510. https://doi.org/10.1590/S0103-84781998000300026

40. Birgel Junior EH, Santos dos MC, de Ramos JAC, Pogliani FC, Birgel DB, Libera AMMPD, et al. Secondary hepatogenous photosensitization in a llama (Lama glama) bred in the state of São Paulo, Brazil. Can Vet J. 2007; 48: 323–324.

41. Opasina BA. Photosensitisation jaundice syndrome in West African Dwarf sheep and goats grazed on Brachiaria decumbens. Trop grassl. 1985; 19: 120–123.

42. De Oliveira CHS, Barbosa JD, Oliveira CMC, Bastianetto E, Melo MM, Haraguchi M, et al. Hepatic photosensitization in buffaloes intoxicated by Brachiaria decumbens in Minas Gerais state, Brazil. Toxicon. 2013; 73: 121–129. https://doi.org/10.1016/j.toxicon.2013.07.001 PMID: 23850427

43. Brum KB, Haraguchi M, Lemos R. Crystal-associated cholangiopathy in sheep grazing Brachiaria decumbens containing the saponin protodioscin. Pesq Vet Bras. 2007; 27. https://doi.org/10.1590/S0100-736x20070000100007

44. Collett MG. Bile duct lesions associated with turnip (Brassica rapa) photosensitization compared with those due to sporidesmin toxicity in dairy cows. Vet Path. 2014; 51: 986–991. https://doi.org/10.1177/0300985813513002 PMID: 24280939

45. Minervino AHH, Júnior RAB, Rodrigues FAML, Ferreira RNF, Reis LF, Headley SA, et al. Hepatogenous photosensitization associated with liver copper accumulation in buffalos. Res Vet Sci. 2010; 88: 519–522. https://doi.org/10.1016/j.rvsc.2009.12.005 PMID: 20064649

46. Sargison ND, Baird GJ, Sotiraki S, Gilleard JS, Busin V. Hepatogenous photosensitisation in Scottish sheep casued by Dicrocoelium dendriticum. Vet Parasitol. 2012; 189: 233–237. https://doi.org/10.1016/j.vetpar.2012.04.018 PMID: 22564662

47. Olinda RG, Medeiros RMT, Dantas AFM, De Lemos RAA, Riet-Correia F. Poisoning by Enterolobium contortisiliquum in cattle in Northeastern Brazil. Pesq Vet Bras. 2015; 35: 44–48. https://doi.org/10.1590/S0100-736x2015000100010

48. Grecco FB, Dantas AFM, Riet-Correia F, Leite CGD, Raposo JB. Cattle intoxication from Enterolobium contortisiliquum pods. Vet Hum Toxicol. 2002; 44: 160–162. PMID: 12046969

49. Green BL, Monlux AW, Panciera RJ. A hepatogenous photosensitivity disease of cattle: I. Experimental production and clinical aspects of the disease. Pathol Vet. 2016; 1: 469–484. https://doi.org/10.1177/030098586400100060
52. Souza PEC, Oliveira SS, Aguiar-Filho CR, Cunha ALB, Albuquerque RF, Evêncio-Neto J, et al. Primary photosensitization in cattle caused by Froelichia humboldtiana. Res Vet Sci. 2012; 93: 1337–1340. https://doi.org/10.1016/j.rvsc.2012.04.005 PMID: 22575746

53. Knupp SNR, Borburema CC, de Oliveira Neto TS, de Medeiros R, Knupp LS, Riet-Correa F, et al. Outbreaks of primary photosensitization in equidae caused by froelichia humboldtiana. Pesq Vet Bras. 2014; 34: 1191–1195. https://doi.org/10.1590/S0100-736X2014001200008

54. Santos DS, Silva CCB, Araújo VO, de Fátima Souza M, Lacerda-Lucena PB, Simões SVD, et al. Primary photosensitization caused by ingestion of Froelichia humboldtiana by dairy goats. Toxicon. 2017; 125: 65–69. https://doi.org/10.1016/j.toxicon.2016.11.258 PMID: 27890773

55. Pimentel LA, Riet-Correa F, Guedes KMR, Macedo JTSA, Medeiros RMT, Dantas AFM. Primary photosensitization in equidae and ruminants in the Brazilian semi-arid caused by Froelichia humboldtiana (Amaranthaceae). Pesq Vet Bras. 2007; 27: 23–28. https://doi.org/10.1590/S0100-736X2007000100005

56. Ivens P. Horses: Hogweed suspected of causing primary photosensitisation in a horse. Vet Rec. 2011; 169: 81–82. https://doi.org/10.1136/vr.d4472

57. Kawada H. Photesthesia in cattle fed the grass, Hypericum erectum. J Jpn Vet Med Assoc. 1980; 33: 372–375.

58. Chabchoub A, Landolisi F, Lasfar F, Amira A, Bousrih A. Photosensitization and keratitis in the Arabian thoroughbred horse. Rev Med Vet. 1999; 150: 617–624.

59. Golder HM, Moss N, Rogers G, Jackson B, Gannon N, Wong P, et al. Acute photosensitisation and mortality in a herd of dairy cattle in Tasmania. N Z Vet J. 2017; 65: 39–45. https://doi.org/10.1080/00480169.2016.1232181 PMID: 27593392

60. Flöck M, Baumgartner M, Bago Z, Schilcher F. Photosensitivity due to liver fluke disease in cattle. Tier Prax. 2003; 31: 143–149.

61. Stafford KJ, West DM, Alley MR, Waghorn GC. Suspected photosensitisation in lambs grazing birds-foot trefoil (Lotus corniculatus). N Z Vet J. 1995; 43: 114–117. https://doi.org/10.1136/vr.161.9.312 PMID: 17766813

62. de Araújo VO, Oliveira Neto TS, Simões SVD, da Silva TKF, Riet-Correa F, Lucena RB. Primary photosensitization and contact dermatitis caused by Malachra fasciata Jacq. N.V. (Malvaceae) in sheep. Toxicon. 2017; 138: 184–187. https://doi.org/10.1016/j.toxicon.2017.09.009 PMID: 28918228

63. Ferrer LM, Ortíz A, Loste A, Fernández A, Verde MT, Ramos JJ. Photosensitisation in sheep grazing alfalfa infested with aphids and ladybirds. Vet Rec. 2007; 161: 312–314. https://doi.org/10.1136/vr.161.9.312 PMID: 17766813

64. Van Halderen A, Harding WR, Wessels JC, Schneidner DJ, Heine EW, Van der Merwe J, et al. Cyano-bacterial (blue-green algae) poisoning of livestock in the western Cape Province of South Africa. J S Afr Vet Assoc. 1995; 66: 260–264. PMID: 8691420

65. Jerrett IV, Chinnock RJ. Outbreaks of photosensitisation and deaths in cattle due to Myoporum aff. Insulare R. Br. toxicity. Aust Vet J. 1983; 60: 183–186. PMID: 6626066

66. Wisloff H, Wilkins AL, Scheier E, Flåøyen A. Accumulation of sapogenin conjugates and histological changes in the liver and kidneys of lambs suffering from alveld, a hepatoenous photosensitization disease of sheep grazing Narthecium ossifragum. Vet Res Commun. 2002; 26: 381–396. https://doi.org/10.1023/A:1016298929610 PMID: 12212728

67. Lin SC, Wu YH, Tsai YS, Chang TW, Tsai KR. Studies on the hepatoenous photosensitization of cattle in Taiwan. TW J Vet Med & Anim Hus. 1981; 30: 159–170. https://doi.org/10.1155/2015/5276106

68. Bridges CH, Camp BJ, Livingston CW, Bailey EM. Kleingrass (Panicum coloratum L.) poisoning in sheep. Vet Path. 1987; 24: 525–531. https://doi.org/10.1177/03009858702400609 PMID: 3455080

69. Regnault T. Secondary photosensitisation of sheep grazing bambarra grass (Panicum coloratum var makuakarienase). Aust Vet J. 1990; 67: 419–419. https://doi.org/10.1111/j.1751-0813.1990.tb03040.x PMID: 2085302

70. Riet-Correa F, Haraguchi M, Dantas AFM, Burakovas RG, Yokosuka A, Mimaki Y, et al. Sheep poisoning by Panicum dichotomiflorum in northeastern Brazil. Pesq Vet Bras. 2009; 29: 94–98. https://doi.org/10.1590/S0100-736X2009000100015

71. Johnson AL, Divers TJ, Freckleton ML, McKenzie HC, Mitchell E, Cullen JM, et al. Fall Panicum (Panicum dichotomiflorum) Hepatotoxicosis in Horses and Sheep. J Vet Int Med. 2006; 20: 1414–1421. https://doi.org/10.1111/j.1939-1676.2006.tb00760.x

72. Badiei K, Mostaghni K, Nazifi S, Khodakaram Tafti A, Ghane M, Momeni SA. Experimental Panicum milaceum poisoning in sheep. Small Rumin Res. 2009; 82: 99–104. https://doi.org/10.1016/j.smalrrumres.2009.02.002
73. Nazifi S, Ghane M, Fazeli M, Ghafari N, Azizi S, Mansourian M. Proso millet (Panicum miliaceum) poisoning in Iranian fat-tailed sheep. Comp Clin Pathol. 2009; 18: 249–253. https://doi.org/10.1007/s00580-008-0784-5

74. Button C, Paynter DI, Shiel MJ, Colson AR, Paterson PJ, Lyford RL. Crystal-associated cholangiohepatopathy and photosensitisation in lambs. Aust Vet J. 1987; 64: 176–180. https://doi.org/10.1111/j.1751-0813.1987.tb09677.x PMID: 3632500

75. Lancaster MJ, Vit I, Lyford RL. Analysis of bite crystals from sheep grazing Panicum schinzi (sweet grass). Aust Vet J. 1991; 68: 281. PMID: 1953556

76. Puoli JR, Reid RL, Belesky DP. Photosensitization in lambs grazing switchgrass. Agron J. 1992; 84: 1077–1080. https://doi.org/10.2134/agronj1992.00021962008400060033x

77. Griffiths IB, Douglas RG. Phytophotodermatitis in pigs exposed to parsley (Petroselinum crispum). Vet Rec. 2000; 146: 73–74. https://doi.org/10.1136/vr.146.3.73 PMID: 10674694

78. Collett MG, Thompson KG, Christie RJ. Photosensitisation, crystal-associated cholangiohepatopathy, and acute renal tubular necrosis in calves following ingestion of Phytolacca octandra (inkweed). N Z Vet J. 2011; 59: 147–152. https://doi.org/10.1080/00480169.2011.567966 PMID: 21541890

79. Smith BL, Asher GW, Thompson KG, Hoggarth GK. Hepatogenous photosensitisation in fallow deer (Dama dama) in New Zealand. N Z Vet J. 1997; 45: 88–92. https://doi.org/10.1080/00480169.1997.36001 PMID: 16031961

80. Greenwood PE, Williamson GN. An outbreak of facial eczema in sheep. Aust Vet J. 1985; 62: 65–66. https://doi.org/10.1111/j.1751-0813.1985.tb14241.x

81. Marasas WF, Adelaar TF, Kellerman TS, Minne JA, Van Rensburg IB, Burroughs GW. First report of facial eczema in sheep in South Africa. Onderstepoort J Vet Res. 1972; 39: 107–112. PMID: 4677123

82. Ozmen O, Sahinduran S, Haligur M, Albay MK. Clinicopathological studies on facial eczema outbreak in sheep in Southwest Turkey. Trop Anim Health Prod. 2008; 40: 545–551. https://doi.org/10.1007/s11250-008-9132-7 PMID: 18716912

83. Hansen DE, McCoy RD, Hedstrom OR, Snyder SP, Ballerstedt PB. Photosensitization associated with exposure to Pithomyces chartarum in lambs. J Am Vet Med Assoc. 1994; 204: 1668–1671. PMID: 8050952

84. Edwards JR, Richards RB, Gwynn RVR, Love RA. A facial eczema outbreak in sheep. Aust Vet J. 1981; 57: 392–394. https://doi.org/10.1111/j.1751-0813.1981.tb00534.x

85. McKenzie RA, Dunster PJ, Burchill JC. Smartweeds (Polygonum spp) and photosensitisation of cattle. Aust Vet J. 1988; 65: 128.

86. Schelcher F, Delverdier M, Bezille P, Cabanie P, Espinasse J. Observation on bovine congenital erythropoietic protoporphyria in the blonde d’Aquitaine breed. Vet Rec. 1991; 129: 403–407. https://doi.org/10.1136/vr.129.18.403 PMID: 1767483

87. McAloon CG, Doherty ML, O’Neill H, Badminton M, Ryan EG. Bovine congenital erythropoietic protoporphyria in a crossbred limousin heifer in Ireland. Ir Vet J. 2015; 68: 15. https://doi.org/10.1186/s13620-015-0044-3 PMID: 26140209

88. Black A, Thomsen A. Congenital protoporphyria in Limousin calves. Surv. 2011; 38: 11.

89. Armstrong SC, Jonsson NN, Barrett DC. Bovine congenital erythropoietic protoporphyria in a Limousin calf bred in the UK. Vet Rec. 2002; 150: 608–610. https://doi.org/10.1136/vr.150.19.608 PMID: 12036245

90. Tuyers I, Ellis K. Case report: bovine congenital erythropoietic protoporphyria in a pedigree Limousin herd. Livestock. 2013; 18: 30–33. https://doi.org/10.12968/live.2013.18.2.30

91. Pence ME, Liggett AD. Congenital erythropoietic protoporphyria in a Limousin calf. J Am Vet Med Assoc. 2002; 221: 277–9–240. https://doi.org/10.2460/javma.2002.221.277 PMID: 1218559

92. Giaretta PR, Panzieria W, Galiza GJA, Brum JS, Bianchi RM, Hammerschmitt ME, et al. Seneciosis in cattle associated with photosensitization. Pesq Vet Bras. 2014; 34: 427–432. https://doi.org/10.1590/S0100-736X2014000500007

93. Giaretta PR, Panzieria W, Hammerschmitt ME, Bianchi RM, Galiza GJN, Wiethan IS, et al. Clinical and pathological aspects of chronic Senecio spp. poisoning in sheep. Pesq Vet Bras. Colégio Brasileiro de Patologia Animal; 2014; 34: 967–973. https://doi.org/10.1590/S0100-736X2014001000008

94. Glastonbury JR, Boal GK. Geeldikkop in goats. Aust Vet J. 1985; 62: 62–63. PMID: 3994606
97. Amjadi AR, Ahourai P, Baharsefat M. First report of geeldikko p in sheep in Iran. Arch Inst Razi; 1977. pp. 71–78.

98. Naci Haydardedeoğlu O. Hepatogenous photosensitization in Akkaraman lambs: special emphasis to oxidative stress and thrombocytopenia. Ankara Univ Vet Fak Derg. 2013; 60: 116–122. https://doi.org/10.1501/Vetfak_0000002564

99. Thwait VK, Dixit AA, Mali SK, Gupta R. Berseem induced photosensitization and its therapeutic management in cattle. Int Poli. Intas Pharmaceuticals Ltd; 2013; 14: 228–229.

100. Jesse FF, Ramanoon SZ. Hepatogenous photosensitization in cattle—A case report. Vet World. 2012; 5: 764–766. https://doi.org/10.5455/vetworld.2012.764-766

101. Dent CR, Roje JC. A condition resembling facial eczema in sheep in New South Wales. Aust Vet J. 1967; 43: 71–71. https://doi.org/10.1111/j.1751-0813.1967.tb15072.x

102. Ghamkhar K, Revell C, Erskine W. Biserrula pelecinus L.—genetic diversity in a promising pasture legume for the future. Crop Pasture Sci. 2012; 63: 833. https://doi.org/10.1071/CP12126

103. Riet-Correa F, Medeiros RMT, Schild AL. A review of poisonous plants that cause reproductive failure and malformations in the ruminants of Brazil. J Appl Toxicol. 2012; 32: 245–254. https://doi.org/10.1002/jat.1754 PMID: 22147504

104. Abera D, Jibat T, Sori T, Feyisa A, Beyene T. Assessment of plant and chemical poisoning in livestock in central Ethiopia. J Environ Anal Toxicol. 2014; 4: 1–5. https://doi.org/10.4172/2161-0625.1000215

105. Johnson JH, Jensen JM. Hepatotoxicity and secondary photosensitization in a red kangaroo (Megalaiia rufus) due to ingestion of Lantana camara. J Zoo Wildl Med. 1998; 29: 203–207. PMID: 9732038

106. Woolford L, Fletcher MT, Boardman WSJ. Suspected pyrrolizidine alkaloid hepatotoxicosis in wild southern hairy-nosed wombats (Lasiorhinus latifrons). 2014. pp. 7413–7418. https://doi.org/10.1021/jl405611n PMID: 24708262

107. Steventon CA, Raidal SR, Quinn JC, Peters A. Steroidal saponin toxicity in eastern grey kangaroos (Macropus giganteus): A novel clinicopathologic presentation of hepatogenous photosensitization. J Wildl Dis. 2018; 54: 491–502. https://doi.org/10.7589/2017-03-066 PMID: 29498896

108. Salam KP, Murray-Prior R, Bowran D. A 'Dream' pasture and its comparison with two existing annual pasture legumes for Western Australia: a farmers’ eye view. In: Livestock Research for Rural Development [Internet]. 2010 [cited 4 Nov 2015]. http://www.lrrd.org/lrrd22/9/sala22167.htm

109. Towers NR. Facial eczema—problems and successes in control. Proc N Z Grassl Assoc. 1986; 121–127.

110. Read E, Edwards J, Deseo M, Rawlin G, Rochfort S. Current understanding of acute bovine liver disease in Australia. Toxins (Basel). 2017; 9: 8. https://doi.org/10.3390/toxins9010008 PMID: 28035972

111. Lancaster MJ, Jub TF, Pascoe IG. Lack of toxicity of rough dog’s tail grass (Cynosurus echinatus) and the fungus Drechslera biseptata for cattle. Aust Vet J. 2006; 84: 98–100. https://doi.org/10.1111/j.1751-0813.2006.tb12238.x PMID: 16555557