

# A Case Report of Retracted Publications in Pharmaceutical Science as a Remedy for Research Malpractice

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## ABSTRACT

**Background:** The number of retractions of journal articles has sharply increased in recent decades. **Objectives:** In this case report, excessive retracted publications on the anti-cancer properties of physcion 8-O- $\beta$ -D-glucopyranoside (PG) in recent years were presented and discussed, in comparison with those of physcion. A literature search for technical and review papers on the anti-cancer properties of PG and physcion was conducted *via* Google Scholar and PubMed. PG and physcion are bioactive anthraquinones. In this study, 13 out of 20 papers (65%) and 3 out of 16 papers (19%) on the anti-cancer properties of PG and physcion were retracted, respectively. The main reason for retraction was the copying of figures from previously published papers. None of the notices of retractions highlighted research malpractice. The word 'RETRACTION' printed in red on every page of retracted articles may be a more effective deterrent for authors than retraction notices. **Conclusion:** This case report exemplifies the retraction of publications on the anti-cancer properties of PG and physcion as a form of remedy for research malpractice, only if the process is properly implemented.

**Keywords:** Physcion, Physcion 8-O- $\beta$ -D-glucopyranoside, Anthraquinones, Retraction, Anti-cancer properties.

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## INTRODUCTION

Retraction is the removal of a published article from a journal by the editor when there is clear evidence of unreliable findings, scientific misconduct, or intentional fraud, involving plagiarism of published work, and fabrication or falsification of text, data or images.<sup>1,2</sup> Other reasons for retractions included misconduct of authors<sup>1,3</sup> and fake peer reviews.<sup>4</sup> According to the Committee on Publication Ethics (COPE), the main purpose of retraction is to promote integrity in scholarly research and publication, and not to punish the authors.<sup>5,6</sup>

In the last two decades, the number of retractions has increased sharply in China (8,612) and has overtaken United States (3,179).<sup>4</sup> A detailed review of retracted biomedical and life-science research articles indexed by PubMed revealed that most retractions were attributed to misconduct (67.4%), including fraud or suspected fraud (43.4%), duplicate publication (14.2%), and plagiarism (9.8%).<sup>3</sup> There are two forms of plagiarism in retraction. One is the copying or unattributed use of someone's work. Two is self-plagiarism or recycling part of one's own previous published work, without acknowledgment.<sup>7</sup>

Quinones are colored cyclic compounds comprising a basic benzoquinone chromophore with two carbonyl groups and two C-C double bonds.<sup>8</sup> They can be divided into benzoquinones, naphthoquinones, and anthraquinones with single, two, and three fused benzene rings, respectively. Anthraquinones are the largest group of natural quinones, including emodin, aloemodin, physcion, catenarin, and rhein.<sup>9</sup> They possess a wide range of bioactivities, such as anti-cancer, anti-inflammatory, immuno-suppressive, antimicrobial, anti-allergen, diuretic, cathartic, laxative, vasorelaxant, antioxidant, and phytoestrogen properties.<sup>8,9</sup> *In vitro* anti-cancer activities of anthraquinones include inhibition of cell growth, disruption of cell cycle, induction of apoptosis, and anti-metastasis.<sup>10</sup>

The objectives of this case report are to present and discuss the excessive retracted publications on the anti-cancer properties of Physcion 8-O- $\beta$ -D-glucopyranoside (PG) in recent years, in comparison with those of physcion. The reasons for retraction were discussed.

## Chemistry of Physcion and PG

Physcion, also known as parietin, has a molecular formula of  $C_{16}H_{12}O_5$  and a molecular weight of 284.3 g/mol. The physcion molecule consists of three fused benzene rings (Figure 1). There is a methoxy (-OCH<sub>3</sub>) group at C3 of ring A, and a methyl (-CH<sub>3</sub>) group at C6 and a hydroxyl (-OH) group at C8 of ring B. Two carbonyl (C=O) groups are located at C9 and C10 of the central



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ring C, which also has two C=C double bonds. The molecular structure of physcion is similar to that of emodin except the latter has -OH groups at C1, C3, and C8.<sup>11</sup> Both are yellow in colour. Physcion 8-O-β-D-glucopyranoside (PG) is a major aglycone of physcion with a molecular formula of C<sub>22</sub>H<sub>22</sub>O<sub>10</sub> and a molecular weight of 446.4 g/mol. In the PG molecule, the physcion component is attached to the glucopyranoside moiety at C1 of ring A (Figure 1).

Physcion and PG are natural anthraquinones that are found in plant species of the families Polygonaceae (*Rheum*, *Polygonum*, and *Rumex*) and Fabaceae (*Cassia*).<sup>12,13</sup> They possess a variety of pharmacological properties such as anti-cancer, hepatoprotective, anti-inflammatory, and anti-microbial activities.<sup>12</sup> Their anti-cancer properties include induction of apoptosis and autophagy, cell cycle arrest, and suppression of metastasis.<sup>12,13</sup>

### Papers on PG and Physcion

#### PG

The first article on the anti-cancer properties of PG was published in December 2014 by Xie and Yang.<sup>14</sup> To date, a total of 20 papers have been published, of which 13 papers (65%)<sup>15-27</sup> were retracted (Table 1). The remaining seven papers (35%)<sup>14,28-33</sup> were non-retracted. The 13 retracted papers attracted 244 citations (72%), while the seven non-retracted papers had 95 citations (28%).

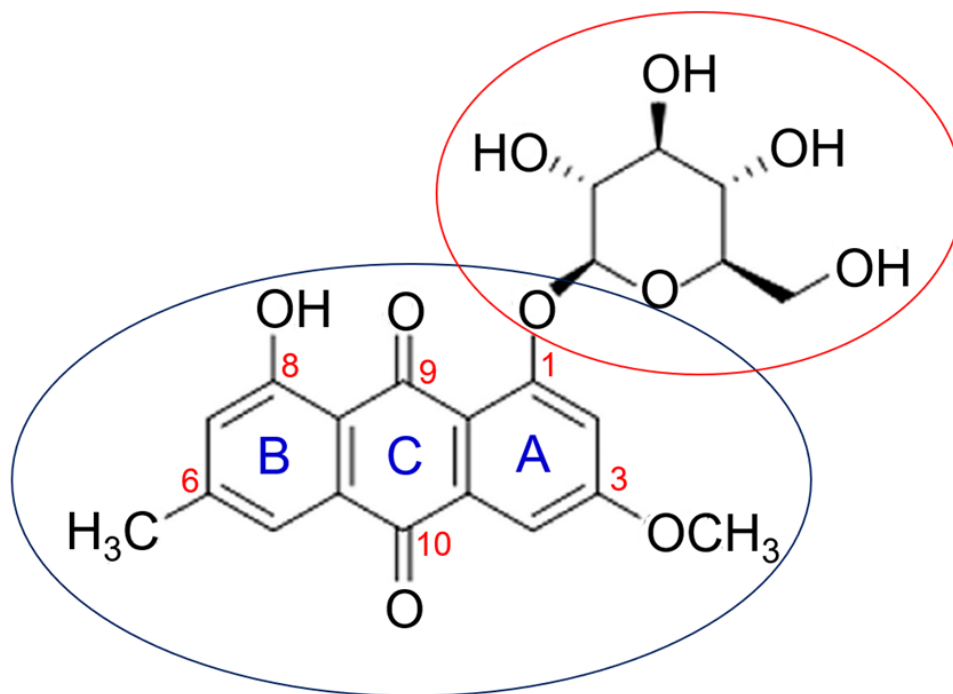
Authors of all 13 retracted PG papers were Chinese scientists from institutions in China. Most of the retraction notices stated

that one or more figures displayed similarities with those of previously published papers.<sup>15,17-22,27</sup> The authors neither provided the raw data for substantiation, nor provided explanations for the similarities, nor cited the references in the reuse of data. Other reasons include the extensive copying of data and text from another source<sup>16</sup> and the scientific integrity of the paper has been compromised.<sup>26</sup> In some of the retraction notices, the editors of journals extended their apologies for not detecting the flaws in the figures during the submission process. For two retracted papers,<sup>23,25</sup> the publishers did not give reasons for the retraction.

Two retracted papers on the anti-cancer properties of PG by Wang *et al.*<sup>15</sup> and Wang *et al.*<sup>22</sup> had the same authors affiliated at the Shandong Provincial Hospital, China. The publication of these two papers in 2016 on hepatocellular carcinoma<sup>15</sup> and in 2018 on renal cell carcinoma<sup>22</sup> suggest repeated attempts at publishing multiple retracted papers by scientists.

Among the 13 retracted papers on the anti-cancer properties of PG, five were published in Biomedicine and Pharmacotherapy (Q1 Elsevier journal with 109 *h*-Index). Journals with two retracted papers each were Pharmacological Reports (Q2 Elsevier journal with 87 *h*-Index), and Anatomical Record (Q2 John Wiley and Sons Inc. journal with 66 *h*-Index). The other journals with single retracted papers were Life Sciences; American Journal of Cancer Research; Naunyn-Schmiedeberg's Archives of Pharmacology; and Artificial Cells, Nanomedicine and Biotechnology.

Journals with seven papers on the anti-cancer properties of PG but not affected by retraction were Neoplasma; Tropical



**Figure 1:** Molecular structure of physcion (encircled in blue) and physcion 8-O-β-D-glucopyranoside (encircled in blue and red).

**Table 1: Types of papers, number and percent of publications, and number and percent of citations on physcion and physcion 8-O- $\beta$ -D-glucopyranoside (PG).**

Compound	Type of paper	Number	Percent	Citation	Percent
PG	Retracted papers	13	65	244	72
	Non-retracted papers	7	35	95	28
Physcion	Retracted papers	3	19	59	14
	Non-retracted papers	13	81	363	86

Journal of Pharmaceutical Research; Journal of Pharmacy and Pharmacology; Acta Pharmacologica Sinica; BMC Complementary and Alternative Medicine; European Review for Medical and Pharmacological Sciences; and Die Pharmazie.

### Physcion

The first two papers on the anti-cancer properties of physcion were in April 2014 by Wijeseka *et al.*<sup>34</sup> and in December 2014 by Hong *et al.*<sup>35</sup> Since then, there were 16 papers on physcion altogether (Table 1). Of these, 13 papers<sup>34-46</sup> were non-retracted (81%), assuming that the journals have adequately checked these papers for malpractice especially plagiarism. The remaining three retracted papers (19%) were by Pan *et al.*,<sup>43</sup> Chen *et al.*,<sup>47</sup> and Pan *et al.*<sup>48</sup> published in European Journal of Pharmacology (Q1 Elsevier journal with 180 *h*-Index); Life Sciences (Q1 Elsevier journal with 164 *h*-Index); and Anatomical Record (Q1 Wiley and Sons journal with 66 *h*-Index); respectively. The three retracted papers were attracted 59 citations (14%) while the 13 non-retracted papers had 363 citations (86%).

Not all papers by the same authors are retracted. For example, two papers by Pan *et al.*<sup>43</sup> and Pan *et al.*<sup>48</sup> from Tianjin Medical Hospital, China, and People's Hospital of Wuhai, China, in 2018 and in 2019 were retracted while another two papers by Pan *et al.*<sup>39</sup> and Pan *et al.*<sup>49</sup> in 2016 and 2018 were not retracted, respectively. This suggests multiple retracted and non-retracted publications by the same group of scientists.

### Review papers

There are two review papers on the anti-cancer properties of PG and physcion, one published in Chemico-Biological Interactions by Liu *et al.*<sup>12</sup> and another published in Current Drug Targets by Adnan *et al.*<sup>13</sup> Together, they attracted 51 citations on PG and 21 citations on physcion. Pending on the extent of plagiarism, these review papers may not be retracted but will have cited retracted papers. In this study, nine retracted physcion papers and seven retracted PG papers were cited by Liu *et al.*<sup>12</sup> and eight retracted physcion papers and 12 retracted PG papers were cited by Adnan *et al.*<sup>13</sup>

## DISCUSSION

In this case report, the main reason for retraction was the copying of figures from previously published papers, according to the retraction notices. The authors did not give explanations for the similarities, nor cite the references when reusing the information, and were not able to provide the raw data for substantiation. Other reasons include the extensive copying of data and text from other sources by one paper,<sup>16</sup> and the scientific integrity has been compromised in another paper.<sup>26</sup>

None of the notices of retraction written by editors highlighted research malpractice in the form of plagiarism, data manipulation or image falsification. The language used was mild, aimed at informing readers of the retraction rather than as a warning to authors not to be involved in future malpractices. Vagueness of retraction statements by editors and a general reluctance to signal research malpractice did little damage to the reputation of offenders.<sup>7</sup> It has been noted that there is often limited information in retraction notices, and a standardized format for reporting retraction notices are needed.<sup>50</sup> The COPE guidelines<sup>5,6</sup> adopted a cautious approach by emphasizing that retraction notices should be objective, factual, and the use of inflammatory language should be avoided. These guidelines might have influenced editors on the cautious choice of words used in retraction notices. As deterrent, editors should use statements such as misconduct since it has been recognized as the main cause of retraction.<sup>1,3</sup>

While it is easier to detect manuscripts for text similarity or plagiarism using available proof-reading software, the detection of falsified or fabricated data or images is much more difficult, sometimes beyond the technical ability of editors. Reviews by peers who are knowledgeable in the field of research are therefore an important component of publication process. Without sound peer reviews, retraction of papers will continue to pose problems for publishers. Editors can also cite the outcomes of peer reviews as reasons for retraction of papers.

In addition to retraction notices, the oblique printing of the word 'RETRACTION' in large, bold, uppercase, and red font on every page of the retracted articles may be a more effective deterrent for authors. The word 'RETRACTION' on every page of a retracted article serves as a red flag emoji, reflecting poorly on the scientific integrity of authors and their affiliations. The use of a watermark

for clear identification of a retracted article<sup>51</sup> and the use of an electronic software for retraction checking<sup>52</sup> are crucial steps.

A retracted article can be revised and republished after removal of the erroneous, falsified, fabricated, or plagiarized content.<sup>53</sup> In this case study, the republication of retracted papers on the anti-cancer properties of PG would not be possible as most authors do not have the raw data for substantiation. The red flag emoji is also a warning sign to the readers and editors. Authors with multiple retracted papers including their affiliations may be black-listed by journals, making their efforts in future publications much more difficult.

## CONCLUSION

In conclusion, this study exemplifies a case report of extensive retraction of publications on the anti-cancer properties of PG and physcion. Multiple retracted papers by the same authors suggest that the retraction process may not be an effective remedy for research malpractice unless stricter regulations are advocated.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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