

Innovations

Efficacy of Collagen Plug for Haemostasis and Socket Preservation after Tooth Extraction: A Systematic Review

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Abstract:

Background: Extraction is a minor surgical procedure performed for therapeutic removal of teeth. Haemostasis is the mechanism of cessation of the extravasation of blood after tooth extraction. Socket preservation is a procedure done to reduce the amount of bone loss post-extraction., **Aim:** To assess the efficacy of Collagen plug as a haemostatic agent and for socket preservation., **Methods:** A literature search, using the MeSH terms – Alveolar bone preservation AND Hemostatics AND Collagen was performed, which includes research papers in databases such as Google Scholar, PubMed, Science Direct, and Wiley, were taken into the study for review, **Results:** Of the 540 articles, after duplicates were removed from the electronic database, a systematic review was carried out and five articles were included in the review. It was found that there was better wound closure and preservation of residual bone in extraction site in patients where collagen plug was placed., **Conclusion:** In the available literature, the use of collagen plug as a haemostatic agent has demonstrated positive outcomes, contributing to enhanced wound healing and reduced postoperative pain and preserving extraction socket to enable that area to receive a prosthesis.

Keywords: Alveolar bone Preservation, Collagen, Hemostatics, Wound healing, Tooth Extraction, Tooth Socket.

Introduction:

Extraction is the procedure of removal of a tooth from the oral cavity with the help of specialized instruments with minimal trauma to the surrounding tissues so that the wound heals uneventfully ^[1]. Bleeding normally occurs after the extraction of the tooth and stops after the clot forms, but in certain cases like patients taking anticoagulants or antiplatelet drugs, the risk of bleeding is higher ^[2].

Haemostasis is the process of coagulation wherein the injured blood vessel wall components trigger a series of reactions by transforming the cells and components of blood into a clot and sealing the injured area [3] [4]. Usually, haemostasis can be achieved mechanically by digital pressure, sutures, or thermally by electrocautery, laser, or by chemical methods like styptics, gelatin sponge, and collagen sponge [5].

Collagen is a vital structural protein in skin, tendons, and bones and is extensively studied for biomedical applications and pharmaceutical products due to its low immunogenicity and high biocompatibility [6]. In dentistry, collagen and its products, including plugs, sponges, and membranes, significantly contribute to tissue regeneration, and wound healing, and act as vital components in materials like membranes and scaffolds for guided tissue regeneration. The biocompatibility of collagen enhances their effectiveness, making them valuable in diverse dental applications [7] [8].

Collagen plug is an absorbable material made of collagen derived from the deep flexor tendon of bovine animals [9]. It is highly porous and controls clot formation in half the time taken by cotton gauze. It works by accumulating platelets to help in clotting. It can also be used to fill defects or voids in bone. It has the advantage of being absorbable and tissue preservation [10]. However, it can cause allergic reactions in some patients or may cause infection in certain cases [11] [12] [13].

Bone remodeling after extraction results in reduced ridge dimension [14]. To avoid this, different socket/ridge preservation techniques are used. The extraction socket in the mandible is restored up to four times faster than the maxilla [15]. Socket preservation is done using bone graft materials that are placed in the extraction site at the time of tooth removal [16].

Objective: To assess the efficacy of collagen plug as haemostatic agent and for socket preservation after tooth extraction.

Materials and Methods:

Study Design:

Systematic review of randomized controlled trials.

ELIGIBILITY CRITERIA:

Inclusion criteria:

- Original articles
- Full- text articles
- Studies which used collagen plug after extraction

Exclusion criteria:

- Articles without full text
- Studies which were done on animals

Search Strategy:

Published literature on the efficacy of collagen plug as a haemostatic agent and its use in socket preservation which includes research papers in databases such as Google Scholar, PubMed, Science Direct, and Wiley were taken into the study for review. A literature to gather the relevant data was performed using the MeSH terms “Alveolar bone preservation, Hemostatics, Collagen”

Search Engine:

- **Google scholar**
- **PubMed**
- **Science Direct**
- **Wiley**

Results: The search yielded 910 records, and 154 articles were assessed independently. Among the 154 articles, five articles were included for the review.

Figure 1 shows the flowchart diagram of the reports identified, duplicates removed, screened, excluded, assessed for eligibility and included in this review.

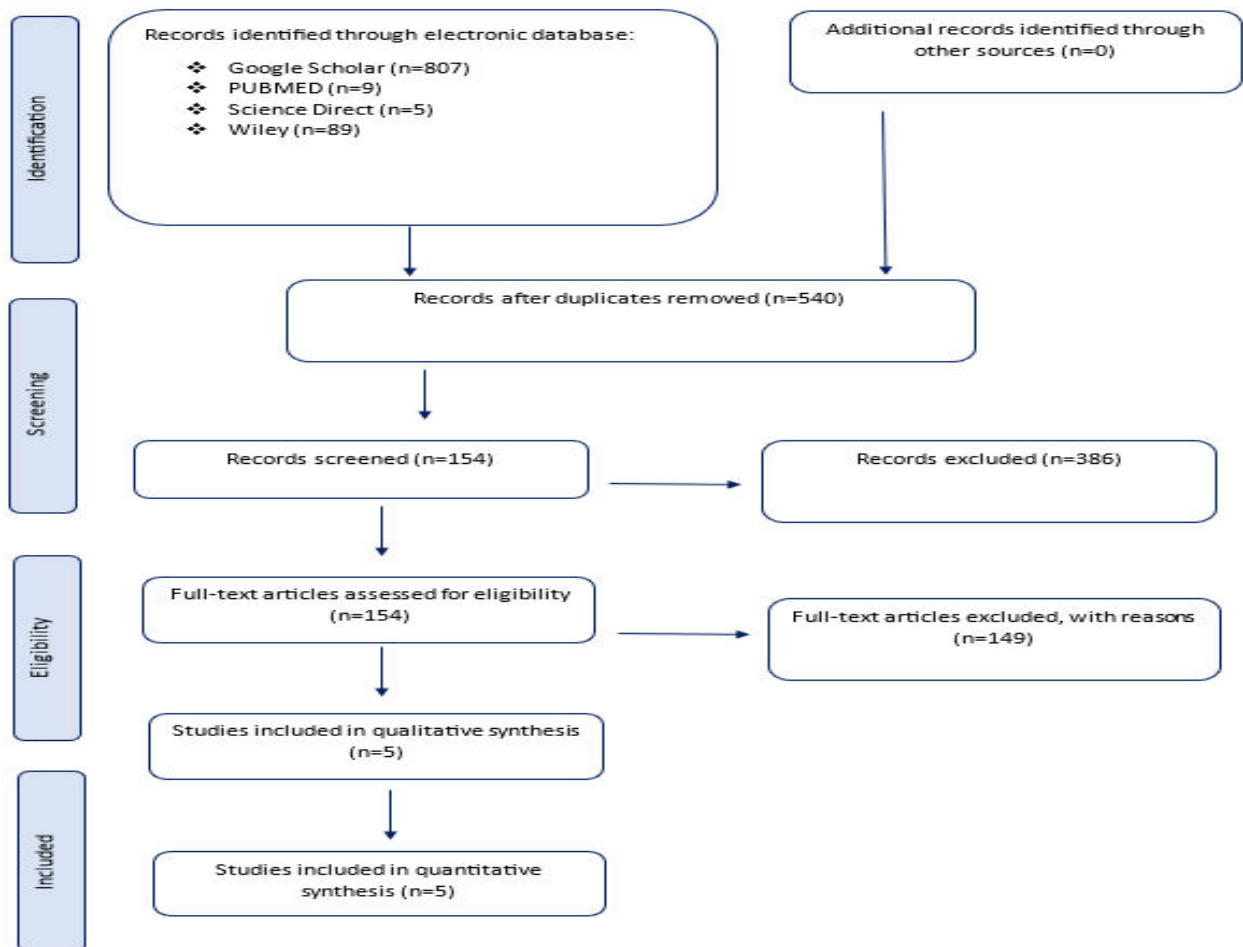


Table 1: Characteristics of the Interventions in the Included Studies

Author Name	Year	Sample Size	Patient Characteristics	Duration	Number (Case/Control)
Dhruv Gupta et al. ^[17]	2012	17	Patient with at least two teeth indicated for extraction which are not adjacent to each other	1 year	Males: 9 Females: 8
Abdelaziz M et al. ^[18]	2015	40	Patient undergoing oral anticoagulant treatment from age 30 -60 years and indicated for simple dental extraction. Oral anticoagulant therapy was not stopped by the physicians.	1 week	GROUP I (Study Group): Non surgical extraction of the tooth followed by the application of CollaPlug in extracted socket and wound suturing – 20 people GROUP II (Control Group): Non surgical extraction of the tooth followed by suturing only – 20 people
Saliba V et al. ^[19]	2019	13	Patient whose age were 18 years and above and had minimum of two teeth in the same jaw to be extracted	May 2019- June 2019 1 month	Males: 7 Females: 6
G Madhan et al. ^[20]	2017	20	Patients above 18 years of age requiring	4 months	GROUP I: Choukroun's PRF

			maxillary anterior teeth extraction followed by implant supported prosthesis		GROUP II: CollaPlug
M Ranganathan et al. ^[9]	2008 - 2009	10	Patients with symmetrical, bilateral impacted mandibular third molars in the age group of 18 – 32 years	1 year	Case group: Bony defect following extraction filled with collagen plug Control group: surgical removal using aseptic protocols

Table 2: Outcome Data as Reported in Included Studies

Author Name	Year	Effect Measure	Results
Dhruv Gupta et al. ^[17]	2012	Student t-test for paired comparisons	Height of ridge: The mean loss of height of ridge was 2.43mm at control sites and 1.45 mm at test sites. The difference between the mean heights of the control and test group also increased from 0.28 mm at baseline to 0.69mm at 6 months. (p-value<0.001) Width of the ridge: Mean loss of width at control sites was 1.68mm and at test site it was 1.07mm.

			Mean difference between the width of the control and test sites increased from 0.32mm at baseline to 0.93mm at 6 months. (p-value<0.001)
Abdelaziz M et al. ^[18]	2015	Chi square test and Monte carlo test used to compare between laboratory investigations of both groups. Wilcoxon signed ranks test for comparing between immediate and each other period.	<p>Immediate postoperative results: Study group: -all 20 cases exhibited mild bleeding grade 2 (G2) on the WHO scale post-application of Collaplug®; only 2 cases showed bleeding grade 1 (G1), and the remaining cases had no bleeding (G0). Control group: - consisting of 20 cases, displayed mild bleeding grade 2 (G2) according to the WHO scale.</p> <p>Intermediate postoperative results (6 hours post-extraction): Study group: - all patients showed no bleeding (G0) on the WHO scale. Control group: -14</p>

		<p>patients exhibited no bleeding (G0), 4 had bleeding grade 1 (G1), and 2 showed bleeding grade 2 (G2).</p> <p>Intermediate postoperative results (48 hours post-extraction): Study group: - 17 cases displayed no bleeding (G0), and 3 cases had grade 1 bleeding (G1). Control group: - 13 cases showed no bleeding (G0), 5 had bleeding grade 1 (G1), and 2 had bleeding grade 2 (G2) according to the WHO scale.</p> <p>Delayed postoperative results: Study group: -18 cases had no bleeding (G0), and 2 cases showed grade 1 bleeding (G1) among the 20 cases. Control group: - exhibited 16 cases with no bleeding (G0) and 4 cases</p>
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			with grade 1 bleeding (G1) on the WHO scale.
Saliba V et al. ^[19]	2019	The Mann-Whitney <i>U</i> test and the Friedman Test were both used for the statistical differences in the pain and the wound healing rates	<p>Mesiodistal healingrate No significant difference was observed between the collagen and xenograft bone groups (P = 0.204), indicating that the collagen group consistently exhibited a higher closure rate compared to the Bio-Oss® group.</p> <p>Buccolingual healing rate - a significant difference between the collagen and xenograft bone groups was noted (P = 0.045). This implies that, by day 14, the collagen group achieved a wound closure rate exceeding 60%, while the Bio-Oss® group did not reach the 60% threshold at that specific time point</p> <p>The pain, as assessed on <i>the</i></p>

			<p><i>Numerical Rating Scale (NRS)</i>, was greater for Bio-Oss®; however, no significant difference was observed between the two procedures over the 7-day period (P = 0.397), except on day 5 (P = 0.004).</p>
G Madhan et al. ^[20]	2017	Analysis of covariance (ANCOVA)	<p>CollaPluggroup:- <i>Baseline mean</i> of 4.67 ± 0.54 and <i>post-mean</i> of 6.98 ± 0.60 for buccal crestal bone level, PRF group :- <i>Baseline mean</i> of 5.43 ± 0.47 and <i>Post-mean</i> of 6.93 ± 0.55. Both groups experienced bone resorption (2.31 mm for CollaPlug and 1.5 mm for PRF), consistent with previous studies. However, there was a statistically significant increase in bone loss in the CollaPlug group compared to the PRF group.</p>
M Ranganathan et al. ^[9]	2008 – 2009	Clinical and Radiographic	<p>Edema: - 1st Day: -</p>

		<p>assessment</p>	<p>Implant side: 6 patients with moderate swelling, 3 with mild, 1 with no obvious swelling. Control side: 1 with severe swelling, 6 with moderate, 3 with mild.</p> <p>1st week: - Implant side: 8 patients with totally reduced swelling, 1 with mild, 1 with moderate. Control side: 6 with no obvious swelling, 4 with mild.</p> <p>2nd Week: - No obvious swelling observed in any patients on both sides.</p> <p>4th week No swelling reported in any patients during clinical follow-up in both groups</p> <p>Pain scoring - No pain, 1 - Mild pain, 2 - Moderate pain, 3 - Severe pain.</p> <p>1st day Implant side: 6 moderate pain, 4 mild pain.</p>
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			<p>Control side: 3 moderate pain, 7 mild pain</p> <p>1st Week: -</p> <p>Implant side: 4 moderate pain, 6 severe pain.</p> <p>Control side: All moderate pain, slight increase for 7 patients.</p> <p>2nd Week: -</p> <p>Implant side: 2 moderate pain, 8 mild pain.</p> <p>Control side: 5 moderate pain, 5 mild pain.</p> <p>4th Week: -</p> <p>Implant side: All cases had no pain.</p> <p>Control side: 7 no pain, 3 mild pain.</p> <p>Wound Gaping: -</p> <p>1st Week-</p> <p>Implant side: Gaping not seen in nine cases, one patient showed gaping</p> <p>Control side: Eight cases showed gaping, two cases had no gaping.</p> <p>2nd Week-</p> <p>Implant side: No cases showed gaping.</p> <p>Control side: Six patients had gaping, four</p>
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							<p>showed no gap.</p> <p>4th Week <i>Implant side:</i> No cases showed gaping. <i>Control side:</i> Gaping seen in two cases.</p> <p>Radiographic Assessment: - 1st Week: - <i>Implant side:</i> Gaping in one patient, no gaping in nine cases. <i>Control side:</i> Gaping in eight cases, no gaping in two cases.</p> <p>2nd Week <i>Implant side:</i> No cases with gaping. <i>Control side:</i> Gaping in six cases, no gap in four cases.</p> <p>4th Week <i>Implant side:</i> No cases with gaping. <i>Control side:</i> Gaping seen in two cases.</p>
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Table 3: Bias Assessment as Included in the Studies

Author Name, Year	Random Sequence Generation	Allocation Concealment	Blinding Of Outcome	Incomplete Outcome Data	Blinding Of Participants And Personnel	Selective Reporting	Judgemental Bias
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Dhruv Gupta et al., 2012 ^[17]	+	?	+	+	-	+	?
Abdelaziz M et al., 2015 ^[18]	?	?	?	+	?	+	-
Saliba V et al., 2019 ^[19]	+	+	-	?	?	+	+
G Madhan et al., 2017 ^[20]	+	?	+	?	-	?	?
M Rangana than et al., 2008-2009 ^[9]	+	+	?	?	-	?	?

+ = Low risk of bias; - = High risk of bias; ? = Unclear risk of bias^{#1}

Discussion

The study by Dhruv Gupta et al. showed that if ridge preservation is done immediately after extraction with the help of a collagen plug then the alveolar bone resorption has been reduced when compared to extraction of tooth alone. The study involved patients with at least two teeth indicated for extraction which are not adjacent to each other. There was a reduction in the loss of ridge height and loss of ridge width when the collagen plug was placed [17].

The study by Abdelaziz M et al. showed that Collaplug® has been established as a successful local haemostatic agent following minor oral surgery in patients undergoing oral anticoagulant therapy. Oral anticoagulant therapy can be maintained during safe extractions with an INR (International Normalized Ratio) < 3. However, for added haemostasis, it is recommended to use Collaplug® before suturing as it is beneficial for controlling postoperative bleeding, especially in sockets resulting from the extraction of posterior maxillary teeth. Furthermore, it contributes to enhanced wound healing and a reduction in postoperative pain [18].

¹+ = Low risk of bias; - = High risk of bias; ? = Unclear risk of bias

The study by Saliba V et al., concluded that collagen appears to be more effective than xenograft, demonstrating superior outcomes in both wound closure and pain management. There was no significant difference in mesiodistal healing rates between collagen and xenograft bone. However, in buccolingual healing rates, collagen significantly outperformed xenograft bone, achieving over 60% closure by day 14, whereas Bio-Oss® did not reach 60% closure by the same day. Even though the pain rating scores between Collagen and Xenograft bone show no notable difference, Bio-Oss® demonstrated higher levels of pain during the seven days post-surgery, particularly on the fifth day [19].

However, the study by G Madhan et al. showed that the PRF excels over CollaPlug for socket preservation due to its simple and cost-effective preparation process. The CollaPlug group also exhibited a notably greater loss of buccal crestal bone compared to the PRF group [20].

The study by M Ranganathan et al showed that the application of CollaPlug™ seems to have beneficial effects on postoperative wound healing in patients, as well as promoting improved bone formation. CollaPlug was utilized as a filler and scaffold to support both bone formation and to promote wound healing in the socket following the surgical extraction of an impacted third molar. Clinical assessment revealed successful healing, with primary closure observed on the side treated with the implant, necessitating no postoperative care. In contrast, the control side required continuous postoperative irrigation of the socket. Radiographic analysis revealed a more rapid bone formation on the implant side in comparison to the control side. Additionally, no intrabony defects were observed distal to the second molar on the implant side. The utilization of this material proved advantageous due to its easy application, cost-effectiveness, and widespread availability, leading to enhanced wound healing and accelerated bone formation [9].

Conclusion :

In conclusion, tooth extraction is a common dental procedure that necessitates careful consideration of various factors, including the bleeding risks associated with anticoagulant use. Achieving haemostasis is crucial for optimal wound healing, and collagen plug has proven effective in controlling clot formation and aiding in socket preservation. The use of collagen plugs as a haemostatic agent, particularly in patients on oral anticoagulants, has demonstrated positive outcomes, contributing to enhanced wound healing and reduced postoperative pain. While studies suggest collagen's effectiveness in wound closure and pain management, conflicting findings with alternative materials like Platelet-Rich Fibrin (PRF) highlight the importance of case-specific considerations. Ultimately, the choice of socket preservation materials should take into account patient condition, cost considerations, and procedural preferences. Although collagen plugs have shown effectiveness, their limitations, such as potential allergic reactions or infections, should be carefully weighed. Dental practitioners should

rely on a comprehensive understanding of the available evidence to make informed decisions in tooth extraction and socket preservation procedures, tailoring approaches to individual patient needs.

Conflict of Interest: Nil

Source of Funding: NIL

Acknowledgements: None

Conflict of Interest: None

References

- [1] G. L. Howe, "Some Complications of Tooth Extraction," *The Annals of The Royal College of Surgeons of England*, 1962:309-323.
- [2] Nagraj SK, Prashanti E, Aggarwal H, Lingappa A, Muthu MS, Krishanappa SK, Hassan H. Interventions for treating post-extraction bleeding. *Cochrane Database of Systematic Reviews*. 2018(3).
- [3] Periyah MH, Halim AS, Saad AZ. Mechanism action of platelets and crucial blood coagulation pathways in hemostasis. *International journal of hematology-oncology and stem cell research*. 2017 Oct 10;11(4):319.
- [4] LaPelusa A, Dave HD. *Physiology, Hemostasis*. In: StatPearls [Internet]. 2023 May 1. StatPearls Publishing.
- [5] Irfan NI, Zubir AZ, Suwandi A, Haris MS, Jaswir I, Lestari W. Gelatin-based hemostatic agents for medical and dental application at a glance: A narrative literature review. *The Saudi Dental Journal*. 2022 Dec 1;34(8):699-707.
- [6] Wang H. A review of the effects of collagen treatment in clinical studies. *Polymers*. 2021 Nov 9;13(22):3868.
- [7] Lanka Mahesh BD, Kurtzman GM, Shukla S. Regeneration in periodontics: Collagen—A review of its properties and applications in dentistry. *Compendium*. 2015 May;36(5).
- [8] Binlath T, Thammanichanon P, Rittipakorn P, Thinsathid N, Jitprasertwong P. Collagen-based biomaterials in periodontal regeneration: current applications and future perspectives of plant-based collagen. *Biomimetics*. 2022 Mar 24;7(2):34.
- [9] Ranganathan M, Balaji M, Krishnaraj R, Narayanan V, Thangavelu A. Assessment of regeneration of bone in the extracted third molar sockets augmented using xenograft (CollaPlugTN Zimmer) in comparison with the normal healing on the contralateral side. *Journal of Pharmacy & Bioallied Sciences*. 2017 Nov;9(Suppl 1):S180.
- [10] He H, Zhou W, Gao J, Wang F, Wang S, Fang Y, Gao Y, Chen W, Zhang W, Weng Y, Wang Z. Efficient, biosafe and tissue adhesive hemostatic cotton gauze with controlled balance of hydrophilicity and hydrophobicity. *Nature*

Communications. 2022 Jan 27;13(1):552.

- [11] Cho H, Jung HD, Kim BJ, Kim CH, Jung YS. *Complication rates in patients using absorbable collagen sponges in third molar extraction sockets: a retrospective study. Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2015 Feb;41(1):26.*
- [12] Kim JW, Seong TW, Cho S, Kim SJ. *Randomized controlled trial on the effectiveness of absorbable collagen sponge after extraction of impacted mandibular third molar: split-mouth design. BMC Oral Health. 2020 Dec;20:1-9.*
- [13] Niki H, Uchida H, Kubo H, Kakudo K, Shimizutani K, Koseki Y. *Computed tomographic examination of bone healing after placement of collagen sponge matrix in the tooth extraction site. J Osaka Odontol Soc. 2001;64:369-74.*
- [14] Tan WL, Wong LT. *A systematic review of post-extraction alveolar hard and soft tissue dimensional changes in humans: comparison of studies with non-fixed or fixed reference points. HKU Theses Online (HKUTO). 2011.*
- [15] Kotze MJ, Bütow KW, Olorunju SA, Kotze HF. *A comparison of mandibular and maxillary alveolar osteogenesis over six weeks: a radiological examination. Head & Face Medicine. 2014 Dec;10:1-7.*
- [16] Wang HL, Tsao YP. *Mineralized bone allograft-plug socket augmentation: rationale and technique. Implant dentistry. 2007 Mar 1;16(1):33-41.*
- [17] Gupta D, Gundannavar G, Chinni DD, Alampalli RV. *Ridge preservation done immediately following extraction using bovine bone graft, collagen plug and collagen membrane. Int J Oral Implantol Clin Res. 2012;3(8).*
- [18] Abdelaziz M, Shaaban R, Abdelhalim S, Sadaka M. *Effect of collaplug® on the healing of extraction sockets in patients under oral anticoagulant therapy (clinical study). Alexandria Dental Journal. 2015 Dec 1;40(2):166-72.*
- [19] Saliba V, Nader N, Berberi A, Chamoun WT. *Collagen Versus Xenograft Bovine Bone Inserted Into Extraction Sockets: Healing and Pain Management. Journal of Maxillofacial and Oral Surgery. 2022 Dec 1:1-1.*
- [20] Singh M, Madhan G. *Comparison of ability of platelet-rich fibrin vs collaplug in maintaining the buccal bone height of sockets following extractions in 20 patients. Journal of Health Sciences & Research. 2015 Jul 1;8(1):1-6.*