Mechanical Properties of Animal Tendons: A Review and Comparative Study for the Identification of the Most Suitable Human Tendon Surrogates

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Review

Mechanical Properties of Animal Tendons: A Review and Comparative Study for the Identification of the Most Suitable Human Tendon Surrogates

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Abstract: The mechanical response of a tendon to load is strictly related to its complex and highly organized hierarchical structure, which ranges from the nano- to macroscale. In a broader context, the mechanical properties of tendons during tensile tests are affected by several distinct factors, due in part to tendon nature (anatomical site, age, training, injury, etc.) but also depending on the experimental setup and settings. This work aimed to present a systematic review of the mechanical properties of tendons reported in the scientific literature by considering different anatomical regions in humans and several animal species (horse, cow, swine, sheep, rabbit, dog, rat, mouse, and foal). This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method. The literature research was conducted via Google Scholar, PubMed, PicoPolito (Politecnico di Torino's online catalogue), and Science Direct. Sixty studies were selected and analyzed. The structural and mechanical properties described in different animal species were reported and summarized in tables. Only the results from studies reporting the strain rate parameter were considered for the comparison with human tendons, as they were deemed more reliable. Our findings showed similarities between animal and human tendons that should be considered in biomechanical evaluation. An additional analysis of the effects of different strain rates showed the influence of this parameter.

Keywords: tendon; animal tendons; mechanical properties; strain rate; elastic modulus; ultimate stress; ultimate strain; best human tendon surrogate; biomechanics; tendon and ligament injuries

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1. Introduction

Tendon and ligament injuries are significant issues in medicine and biomedical engineering, and remain an open problem. The most commonly observed lesions in humans localize to the rotator cuff, quadriceps, patellar, and Achilles tendons, as well as to knee collateral ligaments.

In this vast research field, the Laboratory of Bio-inspired Nanomechanics at Politecnico di Torino studies the mechanical characterization of tendons and ligaments and their relative repair methods as its main research topics, evaluating innovative repair techniques. The work presented here is intended to highlight the most suitable animal subrogate model for testing traditional repair techniques (such as sutures) according to the human tendon destination, thus avoiding the use of human tissues and their related availability issues.

Indeed, the mechanical validation of novel repair techniques and materials is generally carried out on animal tendons and ligaments. Animal models are preferred in preclinical studies for two main types of research purposes: (i) the evaluation of tissue healing through different strategies (for example after growth factor and stem cell injection) and (ii) suture pattern validation.

The tendon healing process has been investigated in different species, including rats [1], mice [2], rabbits [3], and sheep [4]. Animal shoulder models are used to systematically investigate the factors influencing rotator cuff injury and repair [5]. For example, the rat model developed by Soslowsky et al. [6] is considered as the most suitable rotator cuff model due to its similarity to human anatomy (the presence of an acromial arch) and its range of motion [5]. The determination of the most suitable animal rotator cuff model allows for in vivo simulation to analyze different factors affecting the repair process, thus improving the therapeutic process [7]. Several studies dealing with tissue reconstruction via suture patterns or scaffolds used animal specimens to perform tests, especially horse [8], dog [9], and swine [10] tendons. The consistency of the experimental animal model is mandatory to obtain comparable results. Despite their wide use, by comparing the results of different studies it is evident that the reported material properties—in particular, the ultimate stress and strain values—vary, even when the same animal model is used [11]. This issue seems to be particularly evident for the estimation of the ultimate stress and strain values, which are very important parameters for the laboratory testing of tendon repair devices.

A recent study by Dominik et al. [12] compared the biomechanical properties of human semitendinosus tendons with bovine extensor and porcine flexor tendons for surgical fixation and suture technique validation. They concluded that fresh-frozen bovine extensor and porcine flexor tendons are eligible surrogates for biomechanical in vitro studies of human ligament and tendon repairs [12]. On the other hand, porcine flexor and bovine extensor tendons can be also used as grafts for anterior cruciate ligament (ACL) reconstruction [12].

Other studies have affirmed that the ultimate failure loads of modified Kessler suture repair applied on human, porcine, and ovine tendons are comparable, thus leading us to believe that these tendons are appropriate surrogates to study suturing techniques [10]. However, Hausmann et al. [10] found that sheep tendons seem to be the most suitable animal tendon model for mimicking the biomechanical behavior of human tendons. The mechanical behavior of tendons is highly anisotropic, as they show great mechanical strength only in the parallel fiber direction [13]. Indeed, the tendon tissue anisotropy can be evaluated with direction-dependent experiments, such as compression tests, as suggested by Bol et al., 2015 [14]. The biomechanical characterization of tendon can be assessed using different experimental methods; a widespread approach is based on ex vivo ultimate tensile strength testing. Other related parameters, such as load, deformation, and stiffness, can be obtained using the same method, providing information regarding the mechanical behavior of the tendon sample [11].

Several studies have also focused on the analysis of different factors such as gender, physical activity (exercise or training), and injury or disease. In addition, results can also be influenced by the experimental setup, including the environmental conditions and test protocol [11]. Indeed, it is well documented that the mechanical properties of tendons are affected by a considerable number of intrinsic and extrinsic individual factors, including anatomical site, age, and loading history [11]. Certainly, despite common features, tendons from different locations within the body show remarkable variations in terms of their morphological, molecular, and mechanical properties, which are related to their specific function [15]. For example, tendons that experience relatively high physiological stresses and have a spring function during locomotion, such as Superficial Digital Flexor Tendon (SDFT) and Deep Digital Flexor Tendon (DDFT) in horses, develop different mechanical properties from those that experience only relatively low tension stresses, such as Common Digital Extensor Tendon (CDET) [16].

Two factors were reported in the current biomechanical studies: (i) the strain rate value set during the test and (ii) the preconditioning before testing. The tendon is wellknown to be a viscoelastic material, whose behavior is nonlinear and time-dependent [17]. Indeed, due to its time dependency, tendon tissue responds in different ways to strain rate variations during tensile tests; for instance, an increase in the stress and strain at failure has been observed when the strain rate increases [18].

The main purpose of this study was to analyze the biomechanical properties of tendons, such as the elastic modulus, the failure stress, and the failure strain, based on the literature considering several tendons in different animal species (ovine, bovine, swine, rabbit, rat, mouse, and equine) and compare them with those obtained from humans. Specifically, the comparison was made between animal tendons and the following human tendons:

1. Finger extensors: extensor indicis (EI) and digitorum (ED);
2. Finger flexors: digitorum superficialis (FDS), profundus (FDP), and pollicis longus (FPL);
3. Long head of biceps (LHB);
4. Anterior supraspinatus, middle supraspinatus, and posterior supraspinatus;
5. Anterior tibialis tendon (ATT) and Achilles tendon (AT).

In addition, an analysis was conducted to investigate the strain rate influence on the tendons' mechanical properties.

2. Materials and Methods

2.1. Eligibility Criteria

The goal of this systematic review was to collect tensile testing mechanical property values as reported in peer-reviewed studies available in the scientific literature considering different animal species (equine, bovine, swine, ovine, rabbit, dog, mouse, and rat) and compare them to the mechanical behavior of human tendons. The final aim was to define the most suitable animal model.

The first step for the literature research was to establish general study inclusion and exclusion criteria. Articles were selected only if the mechanical properties of healthy tendons were reported in SI units. Furthermore, for statistical accuracy, the expression of these properties as an averaged value ± standard deviation (SD) was required. Thus, studies reporting compression and shear stress were excluded.

In specific, the following exclusion criteria were applied, removing all studies that: (i) reported tensile test results only in a graphic form or expressed them in units of measure not belonging to SI, to avoid introducing approximation errors; (ii) investigated different sutures in tendon repair technical methods; (iii) evaluated the healing of tendon injury through the application of allografts or autografts or that included the use of different kinds of scaffolds or growth factors; (iv) considered pathological or damaged tendons; (v) analyzed mechanical properties in tendons of animal species which were not considered, such as wallaby or monkey. We considered any peer-reviewed article published in English between 1965 and the current date (January 2021).

2.2. Information Sources and Search

The investigation of the published literature was performed using the Google Scholar, PubMed, ScienceDirect, and PicoPolito (Politecnico di Torino search engine) databases. The keywords "tendon", "animal tendons", "mechanical properties", "elastic modulus", and "ultimate stress" were used in separated searches and in conjunction using the Boolean operators 'AND' and 'OR'. After this step, all the collected data were exported to Microsoft Excel and analyzed. The research was conducted by two of the authors (E.P. and S.P.) working independently, each of them investigating half of the number of articles analyzed and then reviewing them together one by one over three months. This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method.

2.3. Data Items

In this analysis the following mechanical properties were considered: elastic modulus or Young's modulus (MPa), maximal load (N), ultimate stress (MPa), and ultimate strain (%). In addition, in regard to the experimental setup of tensile tests, we reported the preconditioning application and the strain rate value set for the tests.

2.4. Additional Analysis

Where possible, a comparison between the mechanical properties for the same species was performed to analyze the strain rate influence.

3. Results

3.1. Study Selection

The search of published literature conducted via the Google Scholar, PubMed, ScienceDirect, and PicoPolito databases using the keywords tendon, mechanical properties, Young's modulus, and ultimate stress yielded more than 2000 articles. The titles and the abstracts were analyzed to exclude fewer inherent papers, resulting in 113 articles for full-text evaluation. In the same way, a second skimming process showed that 40 out of 113 articles matched perfectly with the aim of this study, while the other 73 articles were focused on the analysis of other parameters (i.e., age; sex; healing process; suture techniques; and the insertion of allografts, autografts, and growth factors) and conditions (i.e., loading history, tendons subjected to treatments including gamma radiation, magnetic resonance imaging (MRI), atomic force microscopy (AFM), and second harmonic imaging microscopy (SHIM)), as shown in Figure 1. Since 20 out of 73 articles reported values of native tendons for reference purposes, they were also considered in this work. Finally, 60 articles were employed to obtain the values of the mechanical properties. In particular, the data were classified in animal species as follows: horse (n = 6), bovine (n = 2), swine (n = 6), ovine (n = 5), rabbit (n = 7), dog (n = 8), rat (n = 10), mouse (n = 5), human (n = 10), and 11-month-old foal (n = 1). Article summaries are illustrated in Table 1.

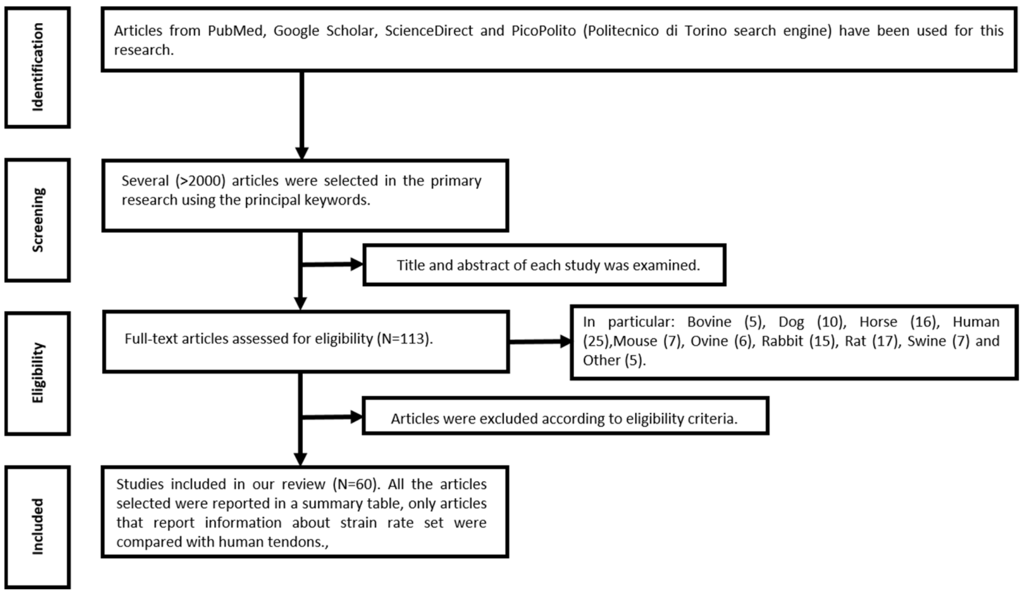

Figure 1. Flow chart of studies identified, reviewed, and excluded from the review.

Table 1. All the selected articles, organized by species.

Animal Species	Studies
Bovine	Domnick et al. (2016) [12], Legerlotz et al. (2010) [11]
Dog	Baker et al. (2012) [19], Dejardin et al. (2001) [20], Derwin et al. (2006) [21], Derwin et al. (2007) [5], Derwin et al. (2009) [22], Balogh et al. (2016) [23], Haut et al. (1992) [24], Liu et al. (2019) [4]
Horse	Batson et al. (2003) [25], Birch (2007) [15], Dowling and Dart. (2005) [26], Dowling et. al (2002) [27], Thorpe et al. (2010) [28]
Mouse	Rigozzi et al. (2010) [29], Dyment et al. (2012) [30], Lin et al. (2005) [31], Gilday et al. (2014) [32], Mikic et al. (2008) [33]
Ovine	Huri et al. (2013) [34], Santoni et al. (2010) [35], Gibbons et al. (1991) [36], Rumian et al. (2009) [37], Salehpour et al. (1995) [38]
Rabbit	Awad et al. (2003) [3], Saber et al. (2010) [39], Young et al. (1998) [40], Juncosa-Melvin et al. (2006) [41], Trudel et al. (2007) [42], Viidik (1969) [43], Yamamoto et al. (1992) [44]
Rat	Eliasson et al. (2007) [45], Lee et al. (2020) [46], Legerlotz et al. (2007) [47], Majewski et al. (2008) [48], Pietschmann et al. (2013) [49], Ferry et al. (2007) [50], Sahin et al. (2012) [51], Su et al. (2008) [52], Lavagnino et al. (2005) [53], Legerlotz et al. (2010) [11]
11-months-old foal	Cherdchutham et al. (2001) [54]
Swine	Domnick et al. (2016) [12], Shadwick (1990) [16], Woo et al. (1981) [55], Smith et al. (1996) [56], Woo et al. (1980) [57], Diehl et al. (2006) [58]
Human	Birch (2007) [15], Carpenter et al. (2005) [59], Itoi et al. (1995) [60], Wren et al. (2001) [61], Lewis and Shaw (1997) [62], Butler et al. (1986) [63], Domnick et al. (2016) [12], Hashemi et al. (2005) [64], Weber et al. (2015) [65], Pring et al. (1985) [66]

3.2. Synthesis of Results

Table 1 shows the selected articles after the verification of the admission criteria, classified by animal species.

3.3. Study Characteristics

Table 2 shows the mechanical properties (loading rate, Young's modulus, maximal load, ultimate stress, and ultimate strain) for different animal species considering strain rate and also the presence of preconditioning. Table 3 shows the same mechanical properties for different human tendons. To analyze the mechanical properties for animal tendons, two data set comparisons were considered. The first set comprised Young's modulus, ultimate stress, and ultimate strain considering the strain rate in mm/s, while the second set dealt with the evaluation of the same parameters considering a strain rate in %/s. For standardization, data reported in mm/minutes were modified to obtain values in mm/s. Data that did not report the strain rate values were not used for graphing and analysis.

For better visualization, all data collected were arranged in different bar graphs that consider a single mechanical property according to strain rate (mm/s and %/s). In particular, to enhance the readability and recognition of the distribution of mechanical properties between the same animal tendon and tendons from different species, and to remark on the similarities between animals and humans, all species were associated with different colors: mouse (mustard-yellow), rat (yellow), dog (green), rabbit (dark green), ovine (azure), bovine (royal blue), swine (navy blue), horse and 11-month-old foal (plum). Regarding the human tendons, these were classified by type, in particular: hand flexor (gray), hand extensor (dark gray), long head of biceps (LHB; orange), and anterior and posterior supraspinatus tendons (dark orange).

Table 2. Mechanical properties of animal tendons. 'na' indicates unavailable data.

Type of Tendon	Species/Breed	Population (n. of Tendons)	Preconditioning	Loading Rate ($mm \cdot s^{-1}$; $mm \cdot min^{-1}$; $\% \cdot s^{-1}$)	Young's Modulus (MPa)	Maximal Load (N)	Ultimate Stress (MPa)	Ultimate Strain (%)	Reference
				Bovine					
Extensor digitorum tendon	na	12	Yes	200 $mm \cdot min^{-1}$	na	1.739 ± 254	na	na	Domnick et al., 2016 [12]
Foot extensor tendon	na	5	na	1$\% \cdot s^{-1}$	714 ± 120	na	na	36 ± 13	Legerlotz et al., 2010 [11]
				Dog					
Infraspinatus tendon (g)	Mongrel	8	Yes	30 $mm \cdot min^{-1}$	na	1.595 ± 285	na	na	Baker et al., 2012 [19]
Infraspinatus tendon (b)	na	6	na	25 $mm \cdot s^{-1}$	na	187 ± 31	na	na	Dejardin et al., 2001 [20]
Infraspinatus tendon (h)	na	9	Yes	10 $mm \cdot min^{-1}$	405.3 ± 86.4	na	na	na	Derwin et al., 2006 [21]
Infraspinatus tendon (h)	Mongrel	8	Yes	6 $mm \cdot min^{-1}$	na	1.349 ± 181	na	na	Derwin et al., 2007 [5]
Infraspinatus tendon (g)	Mongrel	8	Yes	30 $mm \cdot min^{-1}$	na	1.595 ± 285	na	na	Derwin et al., 2009 [22]
Infraspinatus tendon (b)	Mixed breed	14	na	30 $mm \cdot min^{-1}$	na	163.20 ± 61.21	2.60 ± 0.97	na	Liu et al., 2019 [4]
SDFT	na	6	Yes	0.5 $mm \cdot s^{-1}$	101.3 ± 24.0	1721.3 ± 729.9	na	na	Balogh et al., 2016 [23]
DDFT	na	5	Yes	0.5 $mm \cdot s^{-1}$	136.4 ± 52.9	2014.3 ± 229.5	na	na	Balogh et al., 2016 [23]
PT	Medium and large breeds	27	Yes	100$\% \cdot s^{-1}$	474 ± 101	na	na	na	Haut et al., 1992 [24]
				Horse					
SDFT	na	26	Yes	80$\% \cdot s^{-1}$	1086 ± 261	$(10 \pm 3) \cdot 10^3$	110 ± 33	13.1 ± 2.0	Batson et al., 2003 [25]
SDFT	na	12	na	na	970.8 ± 60.4	10.465 ± 410	115.74 ± 4.38	25.98 ± 1.44	Birch et al., 2007 [15]
SDFT	na	na	na	na	1189 ± 63	$(12.4 \pm 1.3) \cdot 10^3$	109.4 ± 8.4	12.5 ± 1.7	Dowling and Dart, 2005 [26]
SDFT	Standardbred	3	No	10 $mm \cdot s^{-1}$	na	7.553 ± 881	65 ± 4.1	17.3 ± 1.2	Dowling et al., 2002 [27]
SDFT	na	38	Yes	80$\% \cdot s^{-1}$	1217.0 ± 199.4	12.379 ± 2 494	128.1 ± 74.7	17.7 ± 3.9	Thorpe et al., 2010 [28]
CDET	na	26	Yes	80$\% \cdot s^{-1}$	1586 ± 279	$(3 \pm 1) \cdot 10^3$	128 ± 42	9.7 ± 2.1	Batson et al., 2003 [25]
CDET	na	12	na	na	1236 ± 209.6	3756 ± 241	136.94 ± 10.44	20.45 ± 1.60	Birch et al., 2007 [15]
				Mouse					
AT (q)	na	10	Yes	10 $mm \cdot min^{-1}$	na	6.0 ± 2.3	10.4 ± 3.9	36 ± 17	Rigozzi et al., 2010 [29]
PT (n)	na	15	Yes	0.003 $mm \cdot s^{-1}$	56.51 ± 18.29	4.13 ± 0.87	11.68 ± 3.38	na	Dyment et al., 2012 [30]
PT (b)	na	12	Yes	0.003 $mm \cdot s^{-1}$	462.8 ± 104.0	na	26.1 ± 7.0	na	Lin et al., 2005 [31]
PT (n)	na	10	Yes	0.003 $mm \cdot s^{-1}$	140.04 ± 19.60	4.73 ± 1.03	17.96 ± 3.09	10.80 ± 2.52	Gilday et al., 2014 [32]
Tail tendon (r)	na	20	na	0.5$\% \cdot s^{-1}$	526 ± 97	na	33 ± 7	7.4 ± 0.81	Mikic et al., 2008 [33]
				Ovine					
(Sheep) Native AT (b)	Merino wether	9	na	25 $mm \cdot min^{-1}$	$(139.6 \pm 46.7) \cdot 10^3$	704.5 ± 85.8	44.2 ± 5.6	na	Huri et al., 2013 [34]
(Sheep) Infraspinatus tendon (e)	Rambouillet–Columbia cross	9	Yes	0.5 $\% \cdot s^{-1}$	na	3516.39 ± 279.61	na	na	Santoni et al., 2010 [35]
(Goat) PT (f)	Mixed breed	24	Yes	100$\% \cdot s^{-1}$	1639.1 ± 435.9	1406.1 ± 363.8	126.8 ± 20.8	15.2 ± 3.9	Gibbons et al., 1991 [36]
(Sheep) PT (b)	Welsh mule	12	Yes	40 $mm \cdot s^{-1}$	373 ± 16.7	$(2.92 \pm 0.075) \cdot 10^3$	76.9 ± 2.66	28.1 ± 0.80	Rumian et al., 2009 [37]
(Goat) PT (b)	Mixed breed	21	Yes	50$\% \cdot s^{-1}$	529.5 ± 109.7	1338.7 ± 463.2	81.4 ± 22.7	20.4 ± 4.2	Salehpour et al., 1995 [38]
				Rabbit					
Flexor tendon (g)	New Zealand	15	Yes	10 $mm \cdot min^{-1}$	1166 ± 281	72.97 ± 14.53	na	na	Saber et al., 2010 [39]
Gastrocnemius tendon (h)	New Zealand	5	na	20$\% \cdot s^{-1}$	337.5 ± 205.8	189.0 ± 26.8	41.6 ± 18.9	na	Young et al., 1998 [40]
AT (h)	New Zealand	8	Yes	30$\% \cdot s^{-1}$	180.0 ± 12.5	390.0 ± 50.0	33.0 ± 4.2	16.0 ± 0.6	Juncosa-Melvin et al., 2019 [41]
AT (b)	New Zealand	10	Yes	10 $mm \cdot s^{-1}$	na	768 ± 16	na	na	Trudel et al., 2007 [42]
AT (b)	na	13	na	na	na	377.4 ± 17.5	na	na	Viidik et al., 1969 [43]

Table 2. *Cont.*

Type of Tendon	Species/Breed	Population (n. of Tendons)	Preconditioning	Loading Rate ($mm·s^{-1}$; $mm·min^{-1}$; $\%·s^{-1}$)	Young's Modulus (MPa)	Maximal Load (N)	Ultimate Stress (MPa)	Ultimate Strain (%)	Reference
PT [(i)]	New Zealand	8	na	2.5 $mm·s^{-1}$	1.581.4 ± 374.9	470.7 ± 67.2	100.7 ± 16.0	7.4 ± 1.5	Awad et al., 2003 [3]
PT [(j)]	Japanese	14	Yes	20 $mm·min^{-1}$	1.390 ± 53	799 ± 40	57.1 ± 2.5	5.1 ± 0.2	Yamamoto et al., 1992 [44]
				Rat					
AT [(k)]	Sprague–Dawley	26	Yes	0.1 $mm·s^{-1}$	179 ± 36	63 ± 5	45 ± 10	na	Eliasson et al., 2007 [45]
AT [(l)]	Sprague–Dawley	15	Yes	3 $mm·min^{-1}$	na	43.3 ± 9.6	na	na	Lee et al., 2020 [46]
AT [(m)]	Sprague–Dawley	20	Yes	1 $mm·s^{-1}$	405 ± 115	48.6 ± 9.7	51.6 ± 10.8	20.5 ± 5.5	Legerlotz et al., 2007 [47]
AT [(n)]	Sprague–Dawley	12	No	1000 $mm·min^{-1}$	na	60–80	na	na	Majewski et al., 2008 [48]
AT [(o)]	Lewis	6	Yes	20 $mm·min^{-1}$	na	52.6 ± 7.8	27.9 ± 8.0	na	Pietschmann et al., 2013 [49]
PT [(b)]	Sprague–Dawley	141	Yes	0.08 $mm·s^{-1}$	na	na	25.7 ± 5.7	31.2 ± 5.9	Ferry et al., 2007 [50]
PT [(o)]	Wistar	8	na	0.1 $mm·s^{-1}$	323.88 ± 56.48	na	30.24 ± 4.41	na	Sahin et al., 2012 [51]
PT [(p)]	Sprague–Dawley	10	Yes	0.05 $mm·s^{-1}$	386 ± 88	55.0 ± 13.6	40.5 ± 8.95	20.0 ± 3.3	Su et al., 2008 [52]
Tail tendon [(b)]	Sprague–Dawley	6	Yes	0.168 $mm·s^{-1}$	312.8 ± 89.5	na	17.95 ± 3.99	7.60 ± 0.99	Lavagnino et al., 2005 [53]
Tail tendon	na	5	na	1$\%·s^{-1}$	1.000 ± 165	na	na	21 ± 7	Legerlotz et al., 2010 [11]
				11-month-old foal					
SDFT [(a)]	Dutch warmblood	6	Yes	4$\%·s^{-1}$	na	na	100 ± 10	11 ± 1	Cherdchutham et al., 2001 [54]
				Swine					
Flexor digitorum profundus tendon	na	12	Yes	200 $mm·min^{-1}$	na	1795 ± 191	na	na	Domnick et al., 2016 [12]
DDFT	na	9	na	5 $mm·min^{-1}$	(1.66 ± 0.16) ·10^3	na	80–90	na	Shadwick et al., 1990 [16]
Digital flexor tendon [(b)]	Yucatan	18	Yes	2 $cm·min^{-1}$	na	(1.63 ± 0.07) ·10^3	na	na	Woo et al., 1981 [55]
Digital extensor tendon	na	9	na	5 $mm·min^{-1}$	(0.76 ± 0.12) ·10^3	na	40–50	na	Shadwick et al., 1990 [16]
Extensor tendon [(c)]	na	12	Yes	0.4 $mm·s^{-1}$	(0.980 ± 0.0943) ·10^3	na	47.29 ± 7.69	6.65 ± 1.23	Smith et al., 1996 [56]
Medial digital extensor tendon [(b)]	Yucatan	18	na	2 $cm·min^{-1}$	na	200 ± 20	na	na	Woo et al., 1980 [57]
Lateral digital extensor tendon [(b)]	Yucatan	18	na	2 $cm·min^{-1}$	na	290 ± 20	na	na	Woo et al., 1980 [57]
AT [(d)]	na	10	Yes	200 $mm·min^{-1}$	248–409	na	42–76	na	Diehl et al., 2006 [58]

[(a)] Values referred to the pastured group. [(b)] Values referred to control group. [(c)] Values referred to the fresh group. [(d)] Values referred to controls for tendons after HHP treatment at 600 MPa. [(e)] Values referred to nine intact contralateral infraspinatus tendons. [(f)] Values referred to the frozen control group. [(g)] Values referred to normal controls (NC) group. [(h)] Values referred to the normal group. [(i)] Values referred to normal central tissue. [(j)] Elastic modulus and ultimate stress values referred to the central portion of the patellar tendon, while stiffness, maximal load, and ultimate strain referred to the whole patellar tendon. [(k)] Values referred to control group for biomechanical evaluation performed after 1 week. [(l)] Values referred to the contralateral normal tendon for FHT (full-thickness harvesting) group. [(m)] Values referred to AMC (age-matched control) group. [(n)] Values referred to normal tendons. [(o)] Values referred to native tendons. [(p)] Values referred to the non-cyclic group. [(q)] Values referred to C57BL/6 (B6) group. [(r)] Values referred to the GDF-7 (+/+) group, i.e., wild type mice that were not deficient in GDF-7.

Table 3. Mechanical properties of the considered human tendons, as retrieved from the literature. 'na' indicates unavailable data.

Type of Tendon	Population	Preconditioning	Loading Rate ($mm \cdot s^{-1}$; $mm \cdot min^{-1}$; $\% \cdot s^{-1}$)	Young's Modulus (MPa)	Maximal Load (N)	Ultimate Stress (MPa)	Ultimate Strain (%)	Reference
				Human				
LHB tendon (s)	7	Yes	100 $mm \cdot min^{-1}$	629 ± 230	305 ± 96.9	45.1 ± 19.6	18 ± 13	Carpenter et al., 2005 [59]
Semitendinosus tendon	12	Yes	200 $mm \cdot min^{-1}$	na	1 406 ± 216	na	na	Domnick et al., 2016 [12]
Anterior supraspinatus tendon	11	na	10 $\% \cdot s^{-1}$	na	411.1 ± 158.8	16.5 ± 7.1	na	Itoi et al., 1995 [60]
Middle supraspinatus tendon	11	na	10 $\% \cdot s^{-1}$	na	152.6 ± 87.5	6.0 ± 2.6	na	Itoi et al., 1995 [60]
Posterior supraspinatus tendon	11	na	10 $\% \cdot s^{-1}$	na	88.1 ± 32.1	4.1 ± 1.3	na	Itoi et al., 1995 [60]
ATT	na	na	na	426 ± 269	(1.54 ± 0.17) $\cdot 10^3$	60.60 ± 9.34	na	Birch et al., 2007 [15]
AT	na	na	na	212 ± 109	(3.87 ± 1.61) $\cdot 10^3$	53.53 ± 19.77	na	Birch et al., 2007 [15]
AT (t)	11	na	1 $mm \cdot s^{-1}$	816 ± 218	4 617 ± 1 107	71 ± 17	7.5 ± 1.1	Wren et al., 2001 [61]
AT (t)	11	na	10 $mm \cdot s^{-1}$	822 ± 211	5 579 ± 1 143	86 ± 24	9.9 ± 1.9	Wren et al., 2001 [61]
AT	16	Yes	10 $\% \cdot s^{-1}$	529.5 ± 109.7	na	73 ± 13	25 ± 3	Lewis et Shaw., 1997 [62]
AT	16	Yes	100 $\% \cdot s^{-1}$	1639.1 ± 435.9	na	81 ± 14	21 ± 1	Lewis et Shaw., 1997 [62]
PT	3	na	100 $\% \cdot s^{-1}$	643.1 ± 53.0	na	68.5 ± 6.0	13.5 ± 0.7	Butler et al., 1986 [63]
PT	20	Yes	100 $\% \cdot s^{-1}$	507.4 ± 135.3	na	58.7 ± 16.3	18 ± 3	Hashemi et al., 2005 [64]
FDS	5	Yes	100 $mm \cdot min^{-1}$	1535.5 ± 747.5	na	127.65 ± 53	10.25 ± 1.5	Weber et al., 2015 [65]
FDP	5	Yes	100 $mm \cdot min^{-1}$	1381.5 ± 677.75	na	109.25 ± 57	10.5 ± 1.25	Weber et al., 2015 [65]
FPL	5	Yes	100 $mm \cdot min^{-1}$	1242 ± 244	na	82.9 ± 12	10 ± 3	Weber et al., 2015 [65]
ED	5	Yes	100 $mm \cdot min^{-1}$	2145.25 ± 808	na	175.75 ± 69	10 ± 1	Weber et al., 2015 [65]
EI	5	Yes	100 $mm \cdot min^{-1}$	1739 ± 781	na	148 ± 59	10 ± 2	Weber et al., 2015 [65]

(s) Failure strain value referred to tendon substance. (t) Values referred to a pooled population group.

3.4. Results of Mechanical Property Evaluation in mm/s

The mechanical properties of tendons from different species showed a uniform distribution as shown for all the mechanical properties (Figures 2–4). In particular, tendons belonging to different anatomical sites of the same species presented very similar results.

However, for the examined human tendons, a different distribution was shown depending on the anatomical site. Differences and similarities between human and animal tendons from different anatomical regions will be highlighted and commented upon. For each one, the best candidates will be determined; a more detailed analysis is reported in the discussion section.

3.5. Results of Mechanical Property Evaluation in %/s

As seen in the previous section, the mechanical properties of tendons from different species showed a uniform distribution, independent of their anatomical region as shown for all the mechanical properties (Figures 5–7). In the case of the mechanical properties evaluated in %/s, human tendons belonging to different anatomical sites showed different mechanical properties with respect to the same tests executed in mm/s, as described in the previous section. As before, the best candidates between human and animal tendons for different anatomical regions will be determined, and a more detailed analysis is reported in the discussion section.

3.6. Results of Additional Analysis—Strain Rate Analysis

The evaluation of the influence of strain rate on the resulting mechanical properties of the tendons was conducted on four animal species (rabbit, rat, mouse, and goat), data reported in Table 4, and the human AT, data reported in Table 5. In particular, there was no clear influence of strain rate on the results. However, changes in mechanical properties in agreement with the literature were found. The influence of strain rate on mechanical properties is discussed thoroughly below.

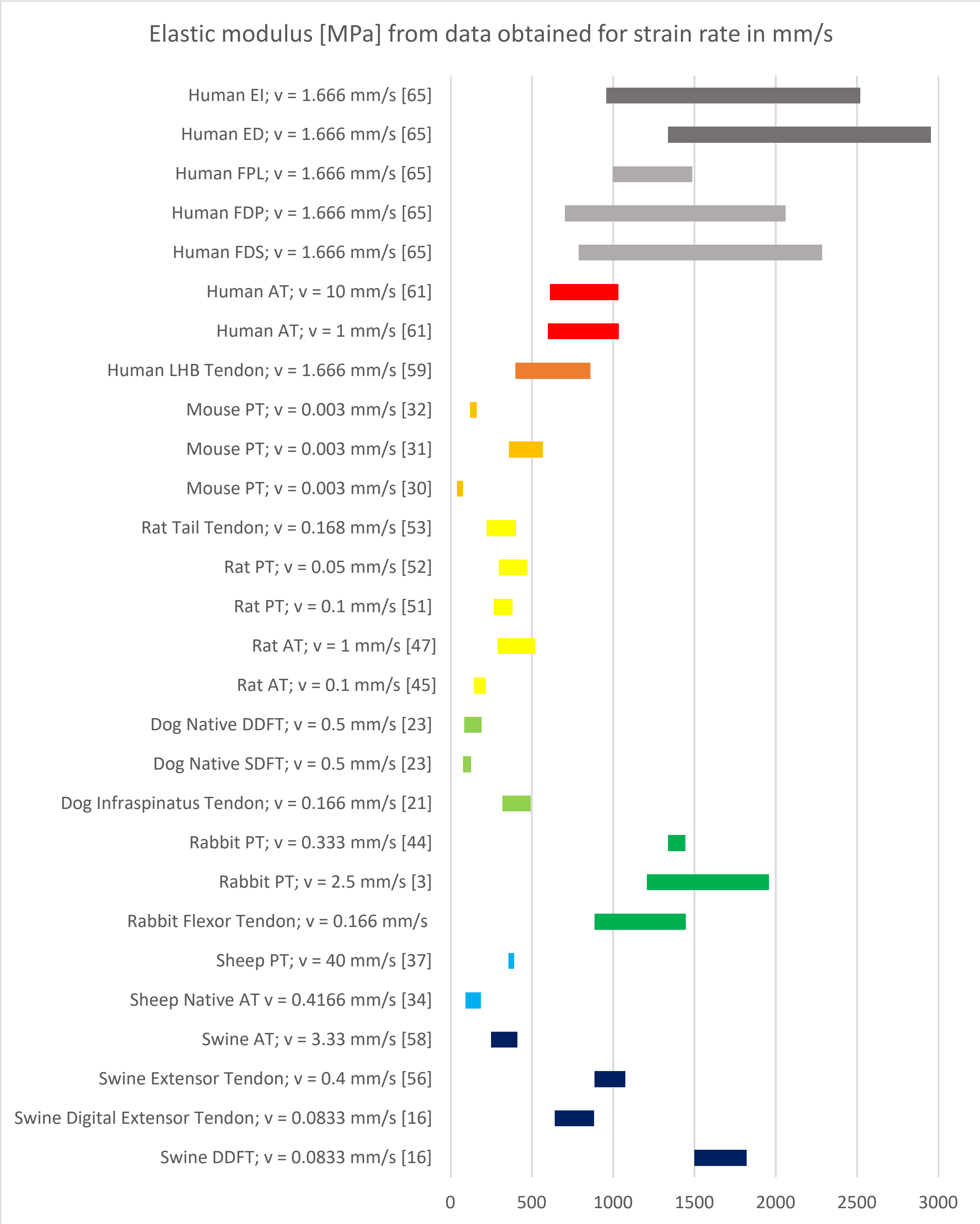

Figure 2. Young's modulus for the considered animal species (mm/s).

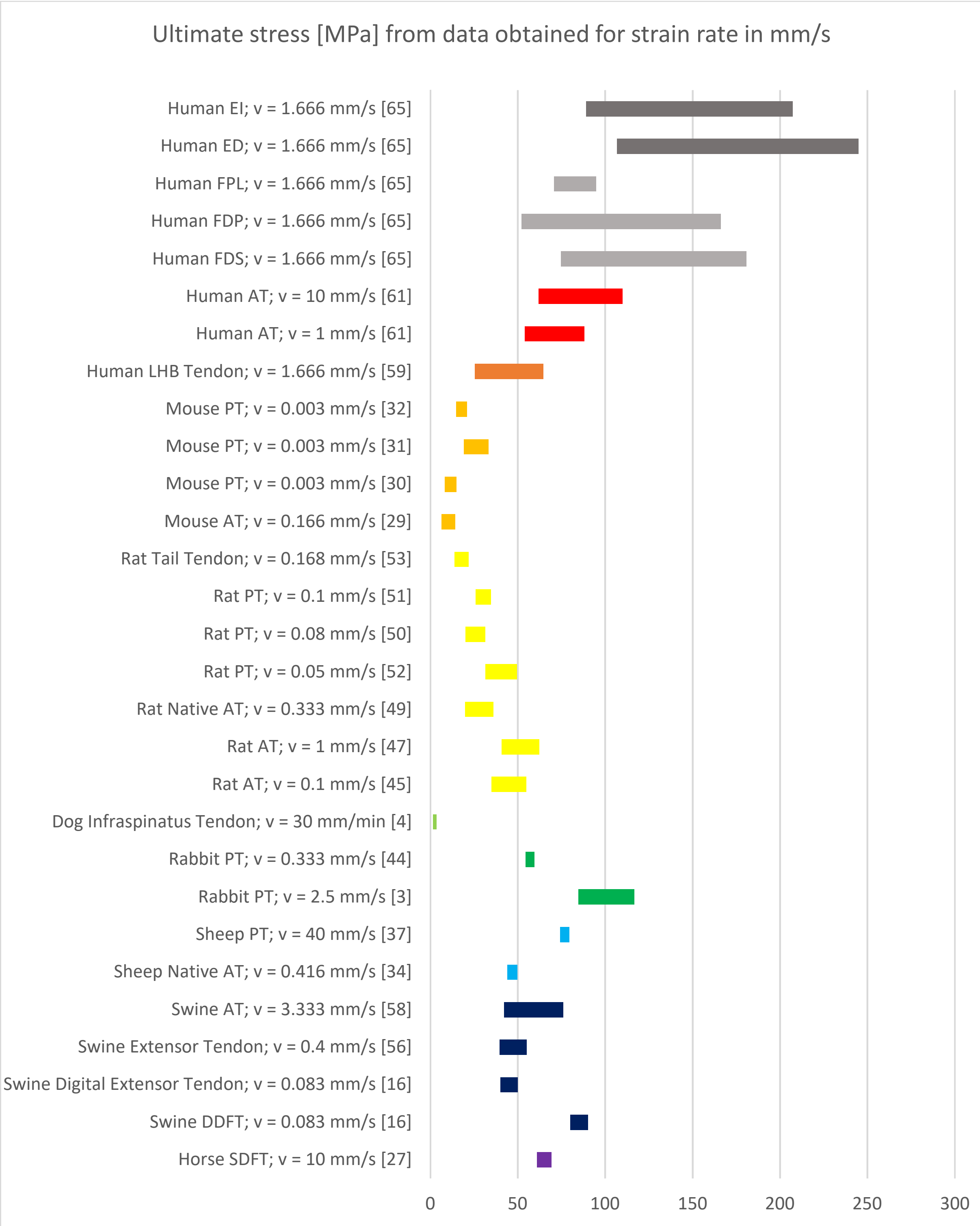

Figure 3. Ultimate stress for the considered animal species (mm/s).

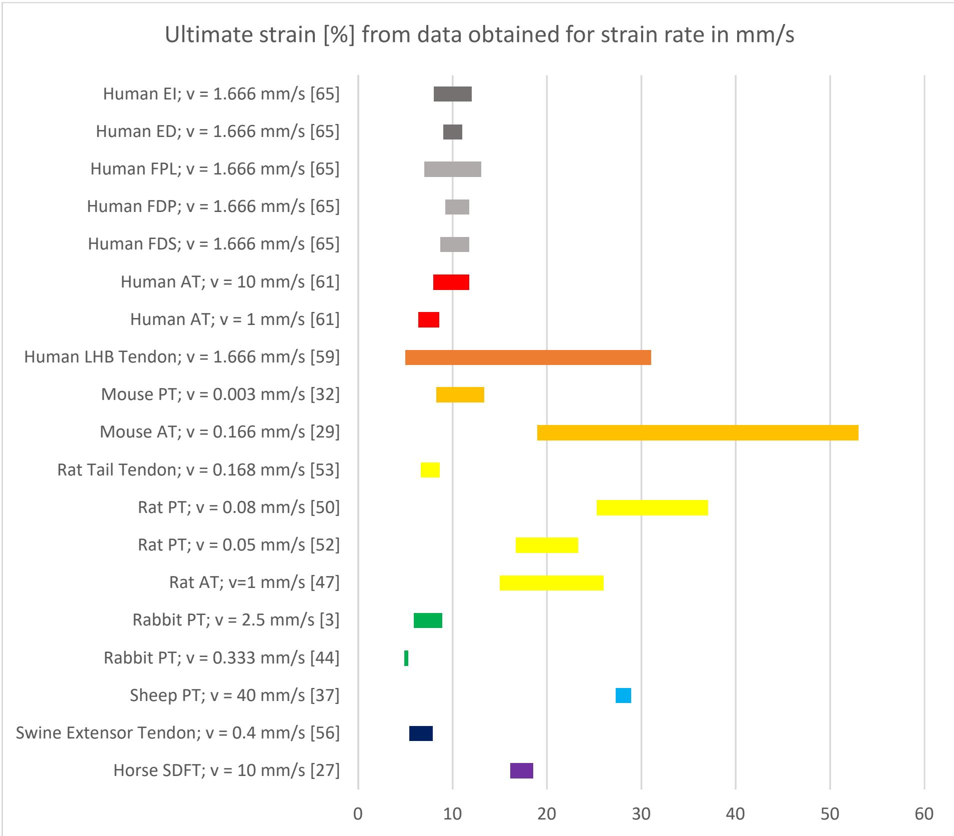

Figure 4. Ultimate strain for the considered animal species (mm/s).

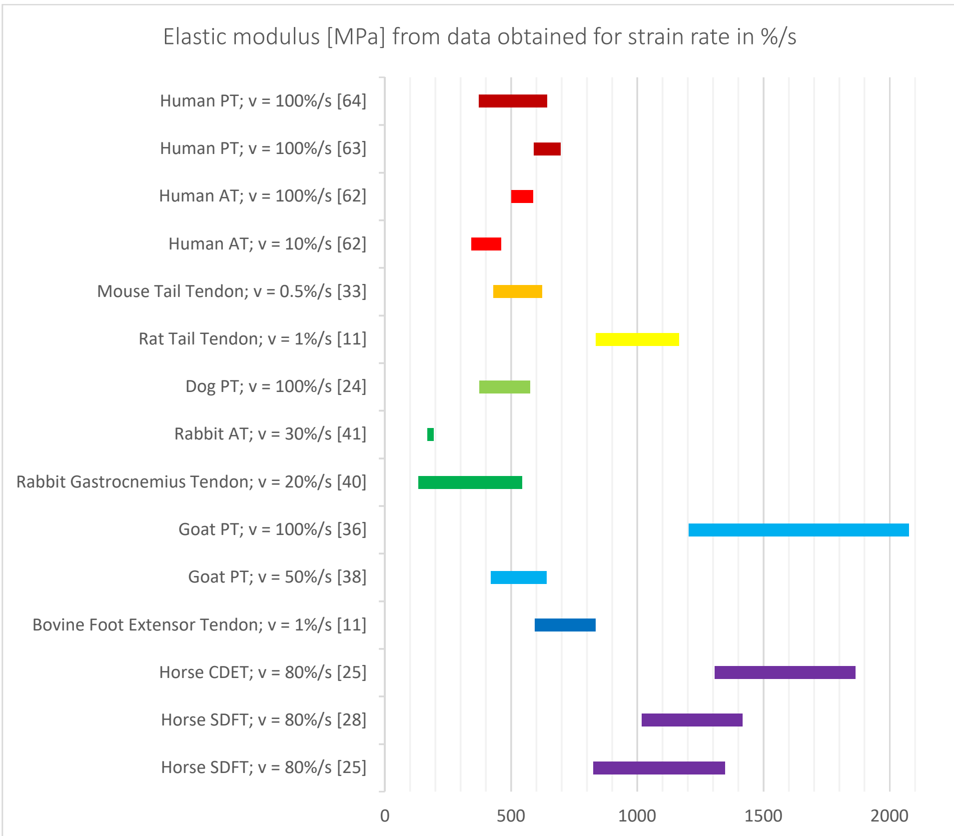

Figure 5. Young's modulus for the considered animal species (%/s).

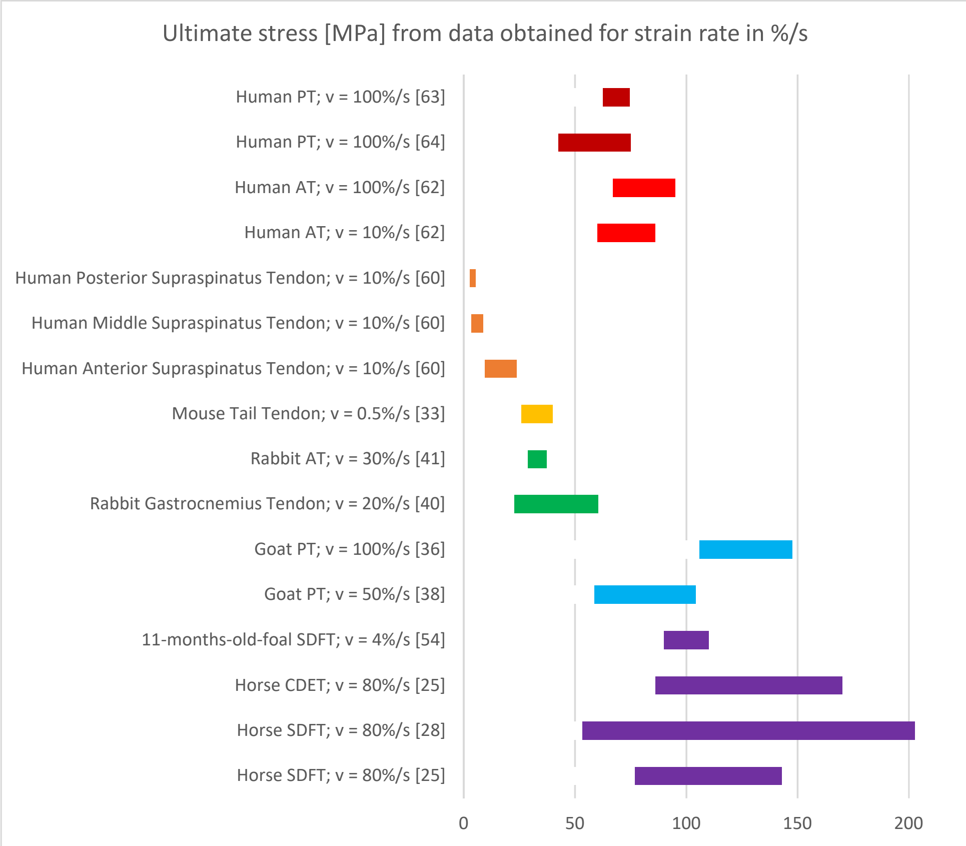

Figure 6. Ultimate stress for the considered animal species (%/s).

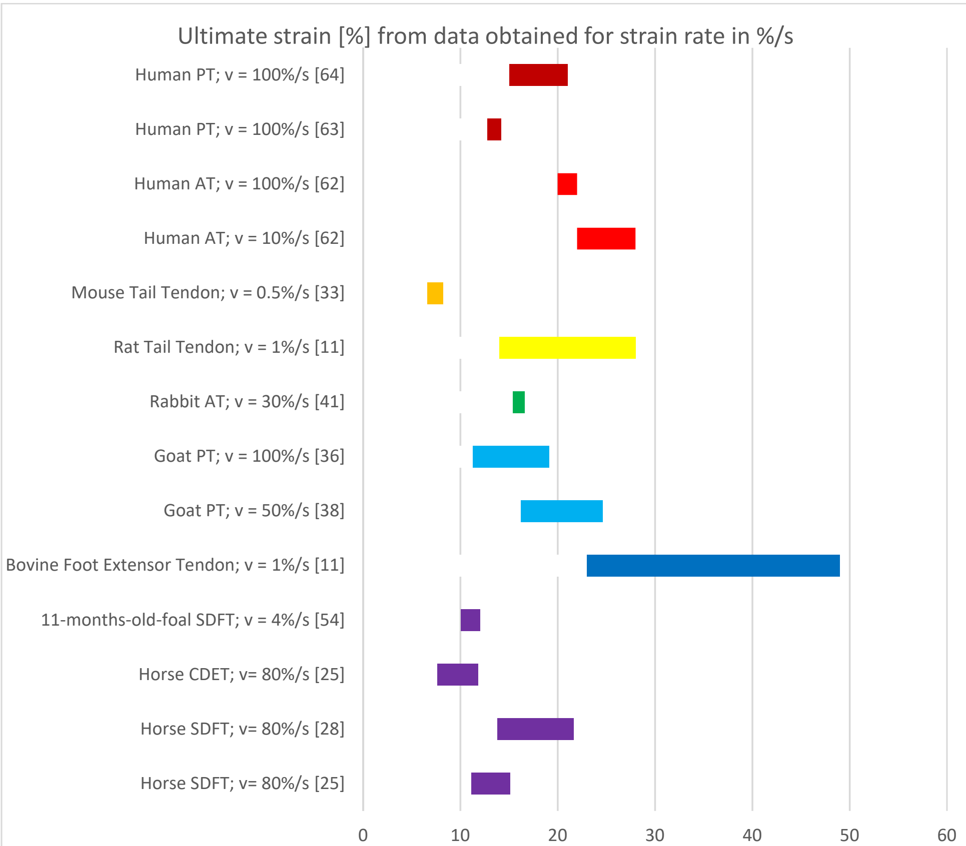

Figure 7. Ultimate strain for the considered animal species (%/s).

Table 4. Influence of strain rate on mechanical properties (mm/s). 'na' indicates unavailable data.

Tendon	Loading Rate ($mm \cdot s^{-1}$)	Young's Modulus (MPa)	Ultimate Stress (MPa)	Maximal Load (N)	Ultimate Strain (%)	Reference
Rabbit PT	0.33	1390 ± 53	57.1 ± 2,5	799 ± 40	5.1 ± 0.27	Yamamoto et al., 1992 [44]
Rabbit PT	2.5	1581.4 ± 374.9	100.7 ± 16	470.7 ± 67.2	7.4 ± 1.5	Awad et al., 2003 [3]
Rat AT	0.1	179 ± 36	45 ± 10	63 ± 5	na	Eliasson et al., 2007 [45]
Rat AT	1	405 ± 115	51.6 ± 10.8	48.6 ± 9.7	20.5 ± 5.5	Legerlotz et al., 2007 [47]
Rat PT	0.05	386 ± 88	40.5 ± 8.95	55 ± 13.6	20.0 ± 3.3	Su et al., 2008 [52]
Rat PT	0.1	323.88 ± 56.48	30.24 ± 4.41	na	na	Sahin et al., 2012 [51]
Human AT	1	816 ± 218	71 ± 17	4617 ± 1107	7.5 ± 1.1	Wren et al., 2001 [61]
Human AT	10	822 ± 211	86 ± 24	5579 ± 1143	9.9 ± 1.9	Wren et al., 2001 [61]

Table 5. Influence of strain rate on mechanical properties (%/s). 'na' indicates unavailable data.

Tendon	Loading Rate ($\% \cdot s^{-1}$)	Young's Modulus (MPa)	Ultimate Stress (MPa)	Maximal Load (N)	Ultimate Strain (%)	Reference
Goat PT	50	529.5 ± 109.7	81.4 ± 22.7	1338.7 ± 463.2	20.4 ± 4.2	Salehpour et al., 1995 [38]
Goat PT	100	1639.1 ± 435.9	126.8 ± 20.8	1406.1 ± 363.8	15.2 ± 3.9	Gibbons et al., 1991 [36]
Human AT	10	401 ± 59	73 ± 13	na	25 ± 3	Lewis et al., 1997 [62]
Human AT	100	545 ± 43	81 ± 14	na	21 ± 1	Lewis et al., 1997 [62]

4. Discussion

The evaluation of the data retrieved from the published scientific literature was performed considering the strain rate with two different units (mm/s and %/s). The analysis only dealt with the comparison between human and animal tendons; thus, no comparison was performed among the mechanical properties of animal tendons.

4.1. Discussion of Results with Strain Rate in mm/s

The human tendons that included in this section are the finger flexor and extensor tendons [65,66], human LHB tendon [59], and Achilles tendon [61].

The mechanical properties of extensor and flexor finger tendons were analyzed by Pring et al., 1985 [66] and Weber et al., 2015 [65] at a strain rate of 100 mm/s. Both studies reported contrasting ultimate strain values; the difference may have been due to samples slipping during the test conducted by Pring et al. [66]. Therefore, in this study, the data from Weber et al., 2015 were used to perform the comparison [65].

The Young's modulus and ultimate strain values obtained by Weber et al., 2015 [65] for EI and ED finger extensors showed similarities with the results obtained for rabbit PT [3]. Conversely, there were no matches for ultimate stress between all the animal species. A partial similarity could be found between swine DDFT [16], rabbit flexor tendon [39], rat tail tendon [53], and mouse PT [32].

Regarding finger flexor tendons (FPL, FDP, and FDS), the Young's modulus and ultimate strain values obtained by Weber et al., 2015 [65] also showed similarities with data obtained for rabbit PT [3]. Moreover, there was a similarity of Young's modulus and ultimate stress values with data reported in swine DDFT [16]; however, a comparison between ultimate strain could not be made as no data were obtained for ultimate strain for this tendon.

Wren et al., 2001 [61] analyzed the mechanical properties of the Achilles tendon with two different strain rate values. For both values, the Young's modulus values were comparable with rabbit flexor tendon [39], swine extensor [56], and swine digital extensor [16]. Concerning the ultimate stress values for both strain rates, the results showed similarities with rabbit PT 3], sheep PT [37], swine DDFT [16], swine AT [58], and horse SDFT [27]. In addition, there was a similarity of ultimate strain for both the strain rate values with mouse PT [32] and rabbit PT [3]; however, the Achilles tendon with a strain rate of 1 mm/s also showed a match with rat tail tendon [53] and swine extensor [67]. Rat and mouse tendons are widely used in medicine to compare with the Achilles tendon in humans. Knockout mice have been used to investigate the composition variation of Achilles tendons from a histological point of view [31]. According to earlier studies evaluating mechanical behavior, contrasting results between rat/mouse and human samples have been obtained [45], which can be observed in our results.

Young's modulus of the LHB tendon, analyzed by Carpenter et al., 2005 [59], showed clear similarities with the results obtained for swine digital extensor tendon [16], and a small similarity was noticed with mouse PT [31], rat AT [47], rat PT [52], and dog infraspinatus [21]. The LHB's ultimate stress [59] showed similarity with results reported for rat AT [45,47,49], rat PT [50–52], rabbit PT [68], sheep AT [34], swine extensor tendon [56], swine digital extensor [16], and swine AT [58]. The ultimate strain results showed similarities with data for mouse PT [32], mouse AT [29], rat AT [47], rat PT [51,53], rat tail tendon [53], rabbit PT [3], sheep PT [37], swine extensor tendon [56], and horse SDFT [27]. There was also a similarity between LHB's mechanical properties and those of the rat AT, rat PT, and swine digital extensor tendon. Indeed, rat and dog shoulder models are used to evaluate the factors that influence human rotator cuff injury and repair processes [5,6,22].

In this study, no similarities were found between human, swine, and bovine tendons; however, Dominick et al., 2016 [12] reported that swine flexor and bovine extensor tendons are eligible surrogates for human semitendinosus tendons in biomechanical studies.

4.2. Discussion of Results with Strain Rate in %/s

The human tendons included in this section are the Achilles tendon [62], patellar tendon [63,64], anterior supraspinatus, middle supraspinatus and posterior supraspinatus [60].

The Young's modulus of the Achilles tendon obtained by Lewis et al., 1997 [62] showed similarities with mouse tail tendon [33], dog PT [24], rabbit gastrocnemius tendon [40], and goat PT [38]. In the same way, a similarity could be noticed between Achilles' ultimate stress and results obtained for rabbit gastrocnemius [40], goat PT [38], 11-month-old foal SDFT [54], horse CDET [25], and horse SDFT [25,28]. The ultimate strain data showed similarities with rat tail tendon [11], goat PT [38], bovine foot extensor [11], and horse SDFT [28]. Essentially, the mechanical properties of the Achilles tendon [62] were comparable with those of rabbit gastrocnemius [40] and goat PT [38]. In fact, the similarities between rabbit gastrocnemius and human Achilles tendons finds confirmation by Young et al. [40] in the evaluation of Achilles tendon repair [37].

The mechanical characterization results for PT from a study conducted by Butler et al., 1986 [63] showed a value of Young's modulus that was similar with mouse tail tendon [33], goat PT [38], and bovine foot extensor [11] values. Similar mechanical results were obtained for human PT by Hashemi et al., 2005 [64]; in this case, there were similarities with dog PT [24] and rabbit gastrocnemius [40]. The results obtained in an additional study conducted by Haut et al. [24] suggest that knee tendon and ligament reconstruction is possible with canine PT, and this finding gives significance to the mechanical evaluation that was performed as the aim of this work.

Regarding the ultimate stress, the values obtained by Butler et al. [63] showed similarities with data from goat PT [38] and horse SDFT [28], while the results of Hashemi et al. [64] showed similarities with rabbit gastrocnemius [40]. There was a clear difference in the PT ultimate strain values obtained in both articles [18,50]. The ultimate strain reported by Butler et al. [63] for PT showed similarities with rat tail tendon [11], goat PT [36], and horse SDFT [25,28]. These results were also found for PT tested by Hashemi et al. [64]; in addition, their results showed similarities with rabbit AT [41] and goat PT [38]. Essentially, the data obtained in both studies presented similarities with the mechanical properties of goat PT [38]. This result is confirmed by the fact that the goat knee model was used to evaluate patellar tendon remodeling [37]. Furthermore, Hausmann et al. [10] reported that sheep tendons seem to be the most suitable animal tendon model for mimicking human tendons; this statement has been proved valid here for PT but not for other human tendons. However, the mechanical properties achieved by PT as tested by Hashemi et al. [64] showed a similar Young's modulus and ultimate stress to data obtained from rabbit gastrocnemius [40], with no ultimate strain data reported for this tendon. This result explains the fact that in literature, the effects of the healing process on knee ligaments and tendons are studied with rabbit knee models [3,45].

Itoi et al., 1995 [60] evaluated the ultimate stress properties of anterior supraspinatus, middle supraspinatus, and posterior supraspinatus tendons. No similarities with animal tendons were found, except for the anterior supraspinatus tendon, which shows slight similarities to rabbit gastrocnemius [40]. Several studies evaluated the healing of rotator cuff tendons in canine animal models; however, no evaluation could be performed for the results obtained in this work [4,22].

4.3. Discussion of Strain Rate Analysis

The analysis of the influence of strain rate on the mechanical properties of tendons did not show univocal results. The mechanical properties of rabbit PT obtained with a velocity of 0.333 mm/s [68] and 2.5 mm/s [3] did not show statistically significant differences for Young's modulus (1390 $\pm$ 53 MPa vs. 1581.4 $\pm$ 374.9 MPa), while ultimate stress (57.1 $\pm$ 2.5 MPa vs. 100.7 $\pm$ 16 MPa) and ultimate strain (5.1 $\pm$ 0.2% vs. 7.4 $\pm$ 1.5%) presented statistically significant differences; in particular, an increment in the values was observed.

Rat AT mechanical properties using a strain rate of 0.1 mm/s [45] and 1 mm/s [47] presented statistically significant differences for Young's modulus (179 $\pm$ 36 MPa vs. 405 $\pm$ 115 MPa, respectively), and this was related to an increase in tissue stiffness. On the other hand, ultimate stress (45 $\pm$ 10 MPa vs. 51.6 $\pm$ 10.8 MPa) did not present statistically significant differences when comparing the two strain rates. No definitive evaluation could be made for the ultimate strain since one article [45] did not report any value for this parameter.

The results obtained by testing rat PT with a strain rate of 0.05 mm/s [52] and 0.1 mm/s [51] showed no statistically significant differences for both Young's modulus (386 $\pm$ 88 MPa vs. 323.88 $\pm$ 56.48 MPa) and ultimate stress (40.5 $\pm$ 8.95 MPa vs. 30.24 $\pm$ 4.41 MPa). Furthermore, no evaluation could be made regarding the ultimate strain, as [51,52] did not report any value. Thus, the increases in strain rate did not cause any changes in the mechanical properties of the tissue. Considering the study of Robinson et al., 2004 [18], the mechanical properties of mouse fascicles with modified and unmodified composition were analyzed according to the strain rate. Robinson et al., 2004 [18] showed that the mechanical properties related to the linear region are strain rate-independent over the range from 0.5%/s to 50%/s; in contrast, the failure properties are highly dependent on strain rate.

The mechanical properties of goat PT with a strain rate of 50%/s [38] and 100%/s [36] showed statistically significant differences for all mechanical properties analyzed. The strain rate increment caused an increase in Young's modulus and ultimate stress; thus, an ultimate strain reduction is advocated, in accordance with the results obtained for rabbit PT.

Concerning human tendons, according to Wren et al., 2001 [61], the influence of strain rate increment (1 mm/s and 10 mm/s) does not cause statistically significant differences in the mechanical properties of Achilles tendons. Several authors have reported that strain rate has an important influence on the mechanical properties at failure (stress and strain); however, once again, there were no statistically significant differences even if a wide range of strain rates was evaluated. However, Abraham et al., 1967 [69] found that for the human Achilles tendon, different strain rates modified the stress magnitude and the shape of the stress–strain curve. In addition, the authors presented a double logarithmic relationship between stress magnitude and strain rate [69].

Herrick et al., 1987 [70] performed some tests on the equine flexor tendon to validate the relationship reported by Abrahams et al. [69]. They found that this relationship might be valid for low strain rate values. In conclusion, the authors affirmed that strain rate has a small and inconsistent effect on stiffness in the range from 5%/s to 50%/s [70].

The study of Lewis et al., 1997 [62] evaluated the effects of a ten times strain rate increase (10%/sec and 100%/sec) on human Achilles tendons. The data reported showed that the strain rate increase produced a statistically insignificant increase in the value of ultimate tensile strength (73 ± 13 MPa vs. 81 ± 14 MPa), a statistically insignificant decrease in the value of ultimate strain (25 ± 3% vs. 21 ± 1%), and a statistically significant increase in Young's modulus (401 ± 59 MPa vs. 545 ± 43 MPa) [62].

In this work, we highlighted how a change in strain rate does not have a unique effect on the mechanical properties of tendons. Analyzing the results of four different tendon tissues (rabbit PT, rat AT, rat PT, and human AT) tested with a strain rate in mm/s, we observed that a strain rate increment caused a significant increase in Young's modulus only in rat AT. A similar result was obtained for human AT by increasing the strain rate by ten times. However, this increase in Youngs' modulus was not statistically significant. In all the other studies, there was no appreciable change in Young's modulus. Considering the four comparisons made for strain rate values in mm/s, we observed statistically significant differences for ultimate stress and ultimate strain in rabbit PT only. In particular, the strain rate increment caused an increase in ultimate stress and a decrease in ultimate strain.

Regarding the effects of the strain rate increase in %/s, the results showed a significant increase in Young's modulus for both goat PT and human AT. This could be due to the application of a drastic increase in the strain rate considering the measurement unit itself; as a result, setting a strain rate of 50%/s results in a tendon deformation of half its initial length in one second, e.g., a strain rate increase in goat PT from 50%/s to 100%/s produces an increment of Young's modulus by three times.

In this context, according to Abrahams et al. [69] a low strain rate increase may have no effect. This evidence, in agreement with our findings, shows that Young's modulus is affected only in the case of a high strain rate increment.

A 10-fold increase in strain rate in human AT [61] did not present statistically significant differences for ultimate stress and strain. However, an increase in ultimate stress and in ultimate strain could be found. Analyzing the strain rate in %/s only for goat PT [36,38] showed statistically significant differences between the results for ultimate stress and ultimate strain, while human AT [62] showed differences, but not statistically significant differences. The increment in strain rate causes an increase in ultimate stress and a decrease in ultimate strain in both tendons.

In conclusion, there is evidence that the value of strain rate can cause a change in the Young's modulus of tendons. Nevertheless, this change in strain rate must be of a significant quantity. The data analysis showed that an increase in strain rate of ten times or greater compared to a reference strain rate value can change the properties of the tissue. The change in strain rate influences tendons' ultimate stress and ultimate strain values. A significant strain rate increase can cause an increase in tendons' ultimate stress and a reduction in ultimate strain.

4.4. Limitations

Despite the comprehensive search across databases, some related articles could have been missed due to the selected keywords and database limitations. This study also did not consider parameters such as animal age, sex, and lifetime activity. These parameters are factors that may influence the biomechanical characteristics of tendons. Additionally, the comparison of tendons should be conducted by evaluating their composition. Future studies should compare the influence of these parameters on the mechanical properties of animal and human tendons, which would lead to a more accurate assessment of the tendon to be used for ex vivo testing. Furthermore, important data might be contained in non-peer-reviewed studies and unpublished theses.

5. Conclusions

Most of the experimental research for human tendon injury and repair is generally performed in animal models, at least in the earliest research stages before human studies. However, animal models have several shortcomings, such as inherent biologic variability, metabolic and hormonal differences between species, and anatomical differences, introducing potential bias to the interpretation of mechanical results during preclinical experiments [31]. As a result, medical, veterinary, and bioengineering researchers must be cautious (i) in applying their results to humans and (ii) in selecting the most appropriate animal tendon for their applications.

This systematic review aimed to define the most suitable surrogate for mimicking the behavior of human tendons when subjected to uniaxial tensile tests. For this purpose, the scientific literature was reviewed extensively, searching for experimental studies involving the mechanical properties of animal tendons, such as Young's modulus, ultimate stress, and ultimate strain. Differences and similarities with human tendons from different anatomical regions were highlighted and commented upon. For each region, the best candidates were determined and discussed.

The key findings obtained in the present review make it evident that different animals tendons show different mechanical properties. Therefore, not every animal tendon can be employed to make a direct comparison to their human counterparts (or to any other human tendon or ligament). The results showed similarities between some animal and human tendons that should be considered in the evaluation of scaffolds and sutures.

Considering the results in mm/s:

- The flexor tendon of the hand (FPL, FDP, and FDS) shows partial similarities for Youngs' modulus and ultimate stress with swine DDFT.
- The extensor tendon of the hand (EI and ED) has similarities with the rabbit PT.
- The LHB tendon shows similarities with the mechanical properties reported for the rat AT, rat PT, and swine digital extensor tendon.

Considering results the obtained for data in %/s:

- The human PT tendon has some similarities with the results obtained for the goat PT.
- The human AT tendon shows comparable mechanical properties with the goat PT, but there are other partial similarities.

However, these results were found only for data in %/s; no clear similarities were visible in the data in mm/s. Thus, it seems highly probable that the choice of strain rate significantly affects the results; unfortunately, different authors reported their results with different settings. Therefore, further studies will be needed to evaluate tendons from different animals and anatomical regions with the same test conditions and strain rate, in a fully comparable way. Future research may enhance the understanding of the best animal tendon species by considering (i) age, (ii) loading history, and (iii) composition.

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