CURRENT CONCEPTS

Pharmacotherapies in Dupuytren Disease: Current and Novel Strategies

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Dupuytren disease is a benign, progressive fibroproliferative disorder of the hands. To date, only one pharmacotherapy (clostridial collagenase) has been approved for use in Dupuytren disease. There is a great need for additional nonsurgical methods that can be used to either avoid the risks of invasive treatments or help minimize recurrence rates following treatment. A number of nonsurgical modalities have been discussed in the past and continue to appear in discussions among hand surgeons, despite highly variable and often poor or no long-term clinical data. This article reviews many of the pharmacotherapies discussed in the treatment of Dupuytren disease and novel therapies used in inflammation and fibrosis that offer potential treatment options. *(J Hand Surg Am. 2023;■(■):■−■.*

Key words Collagenase, Dupuytren, fibrosis, myofibroblast, TGF-beta.

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OUR UNDERSTANDING OF THE mechanisms behind fibroproliferative disorders continues to expand. As a result, newer potential pharmacotherapies in treating diseases such as idiopathic pulmonary fibrosis, scleroderma, Peyronie disease, and Dupuytren disease (DD) are being identified. There has also been renewed interest in repurposing medications already approved by the US Food and Drug Administration (FDA) for the treatment of fibrotic disorders.[1−3] Despite this, the mainstay of treatment for patients with DD is largely surgical. The two most common nonsurgical treatments are local collagenase injections, for enzymatic degradation, and local corticosteroid injections, to reduce inflammatory processes. There is a need for additional pharmacotherapeutic options that are directed toward halting early disease progression or following treatment to prevent recurrence.

The purpose of this article is to provide a summary of currently used and potential new pharmacotherapies in DD. A brief description of the pathophysiology, key signaling cascades, and natural history of the disease are included to set the stage for the need for additional nonsurgical treatments. This article covers many of the medications that have been considered for a repurposed use in DD over the years. Several newer monoclonal antibodies already in use are discussed for their potential antifibrotic and anti-inflammatory role.

NATURAL HISTORY

The typical patient presenting for symptomatic DD demonstrates contracture of the ulnar digits of the

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hand, with the long and ring fingers most often affected. The Hueston table-top test, considered positive when a patient can no longer place their hand and fingers flat on a table, can serve as an indication for intervention. Specific degrees of flexion contraction of 30° at the MCP joint and 15° at the PIP joint also serve as thresholds for the provision of an intervention.[4] As contractures progress, impairment of hand function ensues, with 53° of MCP joint contracture and 77° of PIP joint contracture indicative of critical impairments in hand function.[5]

Current interventional strategies include fasciectomy, percutaneous needle fasciotomy (PNF), and enzymatic digestion. Fasciectomy techniques, including limited fasciectomy and dermatofasciectomy, remain the gold standard, since they have demonstrated high clinical efficacy and low recurrence rates.[4,6,7] Nevertheless, because of their high complication rate as a consequence of their invasiveness, attention has been paid to minimally invasive techniques, such as PNF and enzymatic digestion.

PATHOPHYSIOLOGY

DD is a benign fibroproliferative disorder that affects the palmar fascia of the hand and digits. Its clinical course can involve progressive and symptomatic contractures of the hand and digits, leading to decreased hand function and diminishing quality of life.[7] The natural history of DD can be divided into 3 histologic stages, as initially described by Luck.[8] Stage I, the proliferative phase, is classically characterized by nodule formation within the palmar fascia as well as increased fibroblast activity. Myofibroblasts comprise the majority of cells in the nodule in this phase. Stage II, the involutional phase, is noted by marked nodular thickening and an increase in underlying type III collagen synthesis that becomes oriented along the lines of tension within the palm. Early joint contracture can be seen during this phase. Stage III, the residual phase, is characterized by a large disappearance of myofibroblasts and the replacement of type III collagen with type I collagen (Fig. 1).[9]

Disease progression varies between individuals and can be influenced by established risk factors, such as alcohol intake, smoking, manual labor, diabetes, anticonvulsant drugs, metabolic factors, and genetic predisposition.[9–17] Despite significant research, the underlying genesis of DD has not been clearly elucidated. DD nodules are thought to originate from or near the palmar fascia via mechanisms that include trauma to the palmar fascia, altered immune responses, and/or the presence of oxygen-free radicals.[7] Additionally, the amount and composition of subcutaneous palmar fat may play a role in the progression and recurrence of DD, as lower levels of subcutaneous fat tissue have been noted in individuals with DD.[18–20]

Although the specific mechanisms and triggers for DD development are still yet to be fully elucidated, it is well established that the cell type responsible for DD progression is the myofibroblast. Derived from fibroblasts, the myofibroblast is characterized by the co-expression of high levels of α-smooth muscle actin (α-SMA) and platelet-derived growth factor (PDGF).[21] The clinical contractures seen in DD most likely occur on a cellular level through a contractile apparatus of the myofibroblast containing bundles of actin microfilaments and associated contractile proteins (eg, nonmuscle myosin). Intracellular actin bundles terminate on the myofibroblast surface in the fibronexus, an adhesion complex that incorporates transmembrane integrin proteins to link the actin with extracellular matrix proteins, such as fibronectin fibrils, and adjacent myofibroblasts.[22–26] Extensive research has been performed to better understand the modulators of fibroblasts and myofibroblasts in DD development. Transforming growth factor-β (TGF-β) signaling has been highlighted as critical in DD development.[27] Its specific role in myofibroblast function, DD progression, and potential in treatment is discussed below.

TRANSFORMING GROWTH FACTOR-SIGNALING IN DUPUYTREN DISEASE DEVELOPMENT

Transforming growth factor-β has been implicated in DD development and progression. Three mammalian isoforms of TGF-β exist: TGF-β1, TGF-β2, and TGF-β3. All 3 isoforms have been identified in DD disease nodules, palmar fascia, and cord tissue.[28,29] TGF-β signaling is upregulated in DD and has been shown to be expressed in fibroblasts and myofibroblasts in all 3 histologic stages of DD progression.[28–31] In fibroblasts derived from either DD affected or unaffected tissues, TGF-β upregulates α-SMA expression and induces differentiation of a quiescent fibroblast to a contracting myofibroblast.[9,31–33] The addition of TGF-β in culture models leads to increased contracture of DD fibroblasts.[34] Furthermore, when TGF-β signaling is blocked in DD cells *in vitro*, a dose-dependent decrease in contractility with concomitant decreases in α-SMA and Col1 gene expression and

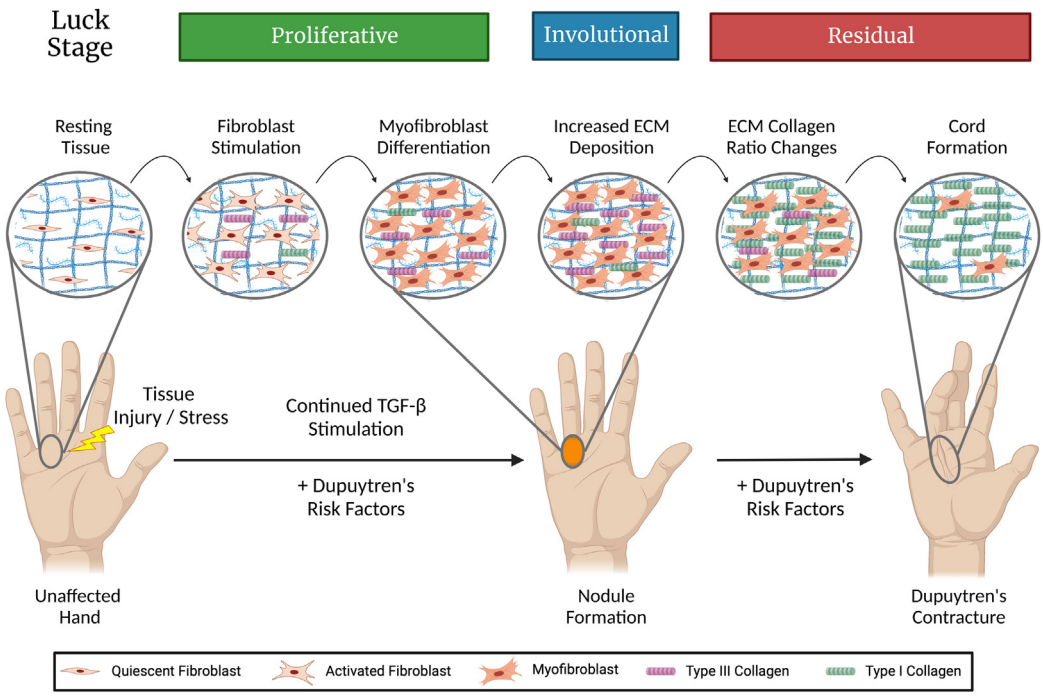

FIGURE 1: Pathophysiology of Dupuytren contracture. Dupuytren disease progression exists on histologic, cellular, and clinical levels. Resting tissue of the unaffected hand contains quiescent fibroblasts. Upon tissue injury or stress, fibroblasts are activated, proliferate, and differentiate into mature myofibroblasts (proliferative stage). With continued TGF-β stimulation and Dupuytren risk factors, disease progresses. Nodule formation occurs as myofibroblasts differentiate and produce extracellular matrix (ECM), with collagen III:I ratio predominating (Involutional stage). The ECM collagen ratio changes to I:III, increased collagen crosslinking occurs, and cellularity decreases as cords form and contraction ensues (residual stage). TGF, transforming growth factor.

α-SMA protein level are seen.[32] Therefore, the ability to block the profibrotic effects of TGF-β signaling in DD is an area ripe for research and clinical potential. Several therapeutic options discussed later in this article target the TGF-β pathway.

CHALLENGES IN STUDYING NEW THERAPIES IN DUPUYTREN DISEASE

To date no single, reliable animal model has been created to study the pathophysiology of DD or the disease response to therapeutics. As a result, researchers have had to rely on a few ways to study the potential efficacy of therapeutics. The first is through *in vitro* studies using fibroblasts isolated from Dupuytren nodules or cords in comparison to fascia overlying the carpal tunnel or the transverse carpal ligament.[32] Key limitations to this approach include the fact that the palmar fascia overlying the carpal tunnel is rarely involved in DD, and the transverse carpal ligament never.[35] Furthermore, because of the paucity of cells isolated from tissue, many experiments expand their cell population through passage 5 prior to performing experiments. However, prior work has shown that by this passage the phenotypes and normal human dermal fibroblasts and mature myofibroblasts tend to converge.[36,37]

The other challenge in studying DD at the clinical level is our reliance on only clinical findings to measure therapeutic efficacy. A noninvasive test to measure the therapeutic effect on Dupuytren tissues in real time is sorely needed. Imaging modalities for monitoring other fibrotic disorders, chiefly idiopathic pulmonary fibrosis, are well described.[38] Noninvasive tests that could be used to study DD are being investigated for other musculoskeletal fibroses. These include modalities such as nuclear magnetic resonance, to assess thickened tissue layers, and ultrasound shear-wave elastography, to assess tissue stiffness.[39]

CURRENT PHARMACOTHERAPIES USED IN DUPUYTREN DISEASE TREATMENT

Enzymatic digestion with collagenase

To date, the only approved pharmacologic therapy that has shown sustained efficacy in treating DD is clostridial collagenase. The underlying mechanism by which *Clostridium histolyticum* collagenases produce their effect is through the degradation of the

collagen found in DD contracture. In 2010, the US FDA approved *C. histolyticum* for injectable use under the name Xiaflex (Auxilium Pharmaceuticals, Inc.).[6,40,41] Xiaflex constitutes 2 purified collagenases (AUX-I and AUX-II) that preferentially degrade collagen types I and III found in DD cords, while sparing collagen types IV and VI that are predominant in vascular basement membranes and perineurium.[41] Treatment takes place over 2 stages, with the first including injection of the diseased DD cord and the second consisting of cord rupture via manual manipulation. Success has been seen in the treatment of MCP and PIP joint contracture, with higher success rates seen in reducing contracture of MCP joints (to within 5° of full extension) than for PIP joints. However, limited data exist for the use of collagenase in early DD as the safety and efficacy data included in the original submission to the FDA for approval were for flexion deformities >20°, in either MCP or PIP joints.[42] Published recurrence rates following collagenase treatment vary widely, with the most cited rate as 35% when defined as a worsening of previously treated contracture >20°.[43] With respect to recurrence rates, enzymatic treatment performs similarly to PNF when used in PIP joints and potentially outperforms PNF when used in MCP joints.[44]

Corticosteroid administration

Corticosteroids, such as injectable triamcinolone, are a common treatment choice for patients with DD.[45–48] Corticosteroids have been shown to decrease rates of cell proliferation in DD nodules and in DD cells cultured *in vitro*,[49] as well as modify disease progression in patients.[46–48] Triamcinolone administration leads to inhibition of TGF-β1 expression and fibroblast apoptosis.[6] Triamcinolone has also been shown to potentiate the activity of collagenase *in vitro*.[50] To our knowledge, no clinical studies have been performed examining the effect of triamcinolone as part of treatment with collagenase. It has been shown that short-term improvements in flexion deformity occur when triamcinolone injection is used in combination with PNF.[51] However, long-term studies are needed to examine whether these effects result in significant long-term recurrence reduction.

REPURPOSED PHARMACOTHERAPIES PROPOSED FOR DUPUYTREN DISEASE

To date, several other pharmacotherapies have been proposed for off-label use in treating DD (Table 1). None have demonstrated either decreased severity or recurrence in long-term clinical trials.[89] For the sake of understanding the rationale for their use they will be discussed here briefly.

Multiple classes of anti-inflammatory and antimitotic medications, in addition to corticosteroids, have been proposed for DD. The nonsteroidal anti-inflammatory (NSAID) celecoxib is being investigated for a role in patients with a high risk of recurrence, while naproxen may have a benefit in reducing postoperative swelling following fasciectomy in patients with DD, although data thus far have been limited and not shown to effect a significant clinical difference.[90] Interferons, both γ and α2b, have the ability to decrease mechanisms behind DD contracture *in vitro*.[57,58] A small pilot study demonstrated the potential to decrease the size of early DD nodules when injected intralesionally.[57] However, no further studies appear in the literature to expand this work. 5-Fluorouracil (5-FU) demonstrated inhibitory effects on Dupuytren myofibroblasts *in vitro*,[60] but showed no beneficial clinical effect when used topically.[61] Systemic colchicine has been reported to improve the severity of penile contractures in Peyronie disease, although without improving concomitant DD contractures.[64]

The anti-oxidants vitamin E and N-acetyl-L-cysteine (NAC) have been investigated for potential roles in DD owing to their ability to abrogate fibrogenesis *in vitro*.[69,91] Vitamin E supplementation was initially described in the 1940s as a potential substitute for surgical therapy in DD.[92] Its utility was refuted by subsequent studies as patients continued to progress despite supplementation.[67,68] NAC has been shown to play a potential role in fibroblast maturation *in vitro*, although it has not been explored as a therapeutic in patients.[70]

Various antihypertensive and vasoactive medications have been described for DD. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II antagonists were proposed owing to their effect in decreasing fibrotic responses *in vitro* and in animal models.[72,73] More recently, Dupuytren tissue has been shown to express angiotensin II receptors.[74] Calcium-channel blockers (eg, verapamil) have been described owing to potential effects on myofibroblast-mediated contracture and the potential to decrease scarring in patients with burns.[75,76] Phosphodiesterase inhibitors (eg, sildenafil) have been proposed as they improve fibrosis via plaque development in animal models with Peyronie disease, another localized fibrotic process.[77–79] Nitric oxide donors (eg, molsidomine) decrease lung fibrosis and Peyronie disease progression in animal models, likely due to the inhibitory effect nitric oxide has on myofibroblast differentiation

TABLE 1. Repurposed Pharmacotherapies Proposed for Dupuytren Disease

Medication	Basic Mechanism of Drug	Proposed Mechanism in DD	In Vitro Results in DD Model	In Vivo Results in Patients with DD	Ref.
Anti-inflammatory					
Corticosteroid	• Nonspecific reduction in collagen synthesis, ECM composition, and proinflammatory mediators[52]	• Decreased fibroblast activity, density, and maturation[52]	• Inhibition of TGF-β1 expression and fibroblast apoptosis[49] • Potentiate activity of collagenase[50]	• Partial DD nodule resolution[47] • Short-term improvements of flexion deformity when used with PNA[51]	46–51,52
Celecoxib	• COX-2 inhibition, downregulation of proinflammatory mediators[53]	• Decreased myofibroblast differentiation through TGF-β signaling pathways[54,55]	• Not tested	• Not tested	53–55
Interferon (IFN)-γ, α2b	• Inhibit cell growth, immunomodulation[56]	• Decreased fibroblast proliferation, myofibroblast differentiation, and collagen production[52,57]	• Decreased fibroblast proliferation and α-SMA expression[57] • Decreased fibroblast contraction[58]	• Decreased early DD nodule size[57]	52,56–58
Antimitotic					
5-Fluorouracil	• Inhibits thymidylate synthase needed for nucleic acid synthesis and function[59]	• Inhibit fibroblast proliferation • Inhibit TGF-β-induced expression of collagen[52]	• Inhibition of myofibroblast proliferation and differentiation[60]	• No clinical benefit when topically applied intraoperatively after limited fasciectomy[61]	52,59–61
Colchicine	• Disrupts cytoskeletal functions by inhibiting β-tubulin polymerization • Inhibits cell proliferation by blocking mitosis	• Decrease collagen synthesis • Increase collagenase activity[62,63]	• Not tested	• No effect on DD contracture when administered orally in Peyronie disease pts[64]	62–65
Anti-Oxidant					
Vitamin E	• Decreases reactive oxygen species	• Decrease myofibroblast differentiation[66]	• Not tested	• No effect when administered orally[67,68]	66–68

(Continued)

TABLE 1. Repurposed Pharmacotherapies Proposed for Dupuytren Disease (Continued)

Medication	Basic Mechanism of Drug	Proposed Mechanism in DD	In Vitro Results in DD Model	In Vivo Results in Patients with DD	Ref.
N-acetyl-L-cysteine (NAC)	• Decreases reactive oxygen species	• Downregulates TGF-β signaling • Decreased production of α-SMA and collagen[69,70]	• Not tested	• Not tested	69,70
Antihypertensive					
ACE inhibitors and angiotensin II antagonists	• Disrupt renin-angiotensin-aldosterone system[71]	• Decrease TGF-β and collagen production[72,73]	• Increased angiotensin II receptors in DD tissue[74]	• Not tested	71–74
Verapamil	• Block voltage-gated calcium channels in cardiac nodes and vessel lining smooth muscle	• Decrease myofibroblast-mediated contracture[75]	• Partially block LPA-promoted contraction of DD fibroblasts[76]	• Not tested	75,76
Vasoactive					
Phosphodiesterase inhibitors	• Inhibits degradation of cyclic GMP by PDE5[77]	• Prevent TGF-β1–induced collagen formation and myofibroblast differentiation[78,79]	• Not tested	• Not tested	77–79
Nitric oxide donors	• Increases release of nitric oxide[77]	• Inhibits TGF-β signaling, collagen synthesis, myofibroblast differentiation[80,81]	• Not tested	• Not tested	77,80,81
Endocrine					
Tamoxifen	• Partial agonist of estrogen receptors	• Modulate TGF-β signaling, decrease fibroblast proliferation and collagen production[82]	• Decreased TGF-β expression in DD fibroblasts, decreased fibroblast contraction[83]	• Short-term improvements after limited fasciectomy, effect lost within 2 years[84]	82–85
Metformin	• Phosphorylate AMP-activated protein kinase, regulating intracellular energy balance[86]	• Reduces TGF-β-induced ECM production in fibroblasts[87]	• Decreased TGF-β-induced contraction of DD fibroblasts[88]	• Not tested	86–88

ACE, angiotensin-converting enzyme; AMP, adenosine monophosphate; COX, carboxylase; DD, Dupuytren disease; ECM, extracellular matrix; GMP, guanosine monophosphate; LPA, lysophosphatidic acid; PDE5, phosphodiesterase 5; PNF, percutaneous needle fasciotomy; Ref., reference; SMA, smooth muscle actin; TGF, transforming growth factor.

and function.[77,80,81,93] Neither phosphodiesterase inhibitors nor nitric oxide donors have been tested in models of DD.

The synthetic nonsteroidal antiestrogen, tamoxifen, modulates TGF-β production, signaling, and fibroblast contractility *in vitro*.[82,83,85] It also results in short-term improvements in patients with DD undergoing limited fasciectomy. However, the gain is lost by two years after treatment and the side effect profile was poorly tolerated.[84] Recently, metformin was proposed as a potential treatment for DD because of its ability to prevent TGF-β–mediated induction of fibroblasts *in vitro*.[86,87] While these results were shown using fibroblasts isolated from samples of patients with DD, no clinical trials demonstrating an effect of metformin in DD have been performed.[88]

CURRENTLY APPROVED THERAPIES TARGETING INFLAMMATION AND FIBROSIS

Several pharmacotherapies with current approval for their anti-inflammatory or antifibrotic effects are under investigation for use in DD (Table 2). The rationale for their use and results to date are discussed below.

Tumor necrosis factor inhibition

Tumor necrosis factor (TNF) is known to play a role in the development and maintenance of the myofibroblast phenotype in DD nodules (Table 2). This has been demonstrated *in vitro* where the addition of TNF, but not other known proinflammatory cytokines (interleukin [IL]-6 and IL-1β), to fibroblasts from samples of patients with DD promoted their differentiation into myofibroblasts.[32] TNF blockade has been performed on DD cells in vitro using the FDA-approved anti-TNF agents, adalimumab and golimumab. Both agents effectively inhibit myofibroblast contraction.[32] These studies have since been corroborated in a proof-of-concept clinical trial. TNF blockade was performed by injection of adalimumab into DD nodules, followed by surgical excision and evaluation. Nodules demonstrated down regulation of the myofibroblast phenotype.[94,95] Most recently, adalimumab injection in early-stage DD resulted in nodule softening and size reduction at one year.[96] Further studies are necessary to assess the long-term utility of TNF blockade in the treatment of DD.

Nintedanib

Nintedanib is one of the two currently used treatments for idiopathic pulmonary fibrosis. Approved for use in the United States in 2014, and in Europe in 2015, Nintedanib is a tyrosine kinase inhibitor with known effects on signaling receptors involved in fibrogenesis, chiefly vascular endothelial growth factor, fibroblast growth factor (FGF), and PDGF.[97] Involvement of PDGF and FGF-mediated signaling has been shown in DD fibroblasts *in vitro*.[33,98] Stimulation of PDGF and FGF signaling pathways can be downstream of TGF-β signaling,[27] which as discussed earlier, plays a role in DD development. Yet, no studies examining the use of Nintedanib for DD have been performed to date. It could be a potential target in DD. However, since Nintedanib does not directly affect TGF-β-mediated fibrogenesis, it may ultimately have limited clinical utility.

Pirfenidone

Pirfenidone (PFD; 5-methyl-1-phenyl-2(1H)-pyridone) is the second most used treatment for idiopathic pulmonary fibrosis. Approved for use in Europe in 2011 and in the United States in 2014, PFD has an inhibitory effect on TGF-β production and TGF-β-mediated fibroblast function and differentiation.[99,100] PFD has been tested in DD fibroblasts *in vitro* and shown to abrogate TGF-β effects including fibroblast proliferation, myofibroblast development, and matrix formation.[101,102] A PFD formulation that could be delivered locally in DD is currently in development.[103]

Tocilizumab and rituximab

It is worth mentioning two additional therapies currently used in cancer and inflammation, and with proposed effects in fibrosis—tocilizumab and rituximab. Tocilizumab is a monoclonal antibody targeting the IL-6 receptor and preventing the binding of IL-6. Although not currently approved for the treatment of fibrosis, it has been suggested based on the known effect of IL-6 on myofibroblast development.[104] Despite the upregulation of IL-6 in cells from DD tissue, neither the addition of IL-6 nor its blockade has shown significant effects on DD cells *in vitro*.[32] Rituximab is a monoclonal antibody targeting the B-cell surface protein CD20, leading to downregulation of B-cell differentiation and antibody formation.[105] Its primary clinical applications include B-cell lymphomas, leukemias, and B-cell mediated autoimmune diseases.[109] While some have suggested a role for autoantibodies in DD,[106–108] a definitive link with CD20-positive cells has not been made.

CONCLUSION

Dupuytren disease remains a challenging clinical entity to treat. While historically accepted and proven therapies such as fasciectomy procedures demonstrate good efficacy of treatment, their risk profile has led to

TABLE 2. Currently Approved Pharmacotherapies in Fibrosis and Inflammation

Medication	Basic Mechanism of Drug	Proposed Mechanism in DD	In Vitro Results in DD model	In Vivo Results in Patients with DD	Ref.
TNF inhibitors (eg, adalimumab)	• Monoclonal antibody targeting and inactivating TNF-α	• Decrease TNF-driven fibroblast differentiation and contraction[32]	• Inhibition of myofibroblast contraction • Reduced α-SMA expression[32]	• Down regulation of myofibroblast phenotype in DD nodules[94,95] • DD nodule softening and size reduction at 1 year[96]	32,94–96
Nintedanib	• Tyrosine kinase inhibitor targeting profibrogenesis signaling (VEGF, FGF, PDGF)[97]	• Decrease fibroblast differentiation by PDGF- and FGF-signaling[33,98]	• Not tested	• Not tested	33,97,98
Pirfenidone	• Inhibits TGF-β production and TGF-β-mediated fibroblast function[99,100]	• Decrease TGF-β-mediated fibroblast function and differentiation[99,100]	• Decreased fibroblast proliferation, myofibroblast differentiation, and matrix production[101,102]	• Not tested • Intradermal formulation being investigated for DD[103]	99–103
Tocilizumab	• Monoclonal antibody targeting IL-6 receptor, preventing binding of IL-6	• Decrease IL-6–mediated myofibroblast development[104]	• No effects on DD cells[32]	• Not tested	32,104
Rituximab	• Monoclonal antibody targeting B-cell surface protein CD20[105]	• Decrease autoantibody contribution to DD[106–108]	• Not tested	• Not tested	105–108

CD20, B-lymphocyte antigen CD20; DD, Dupuytren disease; FGF, fibroblast growth factor; IL, interleukin; PDGF, platelet-derived growth factor; Ref., reference; SMA, smooth muscle actin; TGF, transforming growth factor; TNF, tumor necrosis factor; VEGF, vascular endothelial growth factor.

a search for minimally invasive techniques. Enzymatic digestion and treatment with collagenase have become a staple in DD treatment for over a decade. Despite the addition and broad acceptance of this pharmacotherapy, there is a need of a primary (or adjuvant) therapy modality that can either stop progression in the 30% to 50% of patients in early stages at risk or prevent disease recurrence following treatment.

As fibroproliferation underscores the etiology of DD, it is important to take an antifibrogenic approach to find new pharmacotherapies. This review highlights the pathophysiologic basis of the fibrotic response seen in DD, chiefly through TGF-β signaling. The 2 most used pharmacotherapies in DD today, collagenase for enzymatic digestion of diseased cords as well as corticosteroids for the anti-inflammatory effects, are described. For the sake of providing historical background, many of the medications that have been discussed in articles over years for a repurposed use in DD are covered. Lastly, the article presents several medications with current approval for anti-inflammatory or antifibrotic effects that either are being used or may be considered for use in DD.

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