UNIVERSIDADE DO SUL DE SANTA CATARINA

FERNANDA MENDES DE MORAES

DESENVOLVIMENTO DE UM PÓ HEMOSTÁTICO À BASE DE POLISSACARÍDEOS E AMINOÁCIDOS PARA CONTROLE DE HEMORRAGIAS

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Tubarão

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Trabalho de Conclusão de Curso apresentado ao Curso de Farmácia, da Universidade do Sul de Santa Catarina, como requisito parcial para obtenção do título de Farmacêutica.

Orientadora: Prof ª. Karine Modolon Zepon, Dra.

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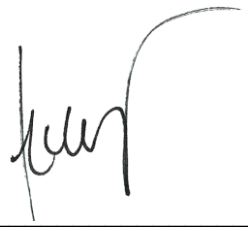
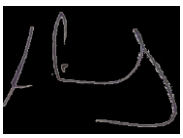
Este Trabalho de Conclusão de Curso foi julgado adequado à obtenção do título de Farmacêutica e aprovado em sua forma final pelo Curso de Farmácia, da Universidade do Sul de Santa Catarina

Tubarão, 30 de novembro de 2020.



Profª. e Orientadora Karine Modolon Zepon, Dra.
Universidade do Sul de Santa Catarina



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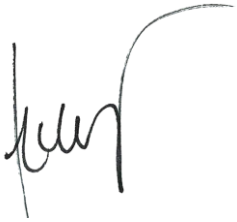
AGRADECIMENTOS

Em meio ao antigo cenário de aulas presenciais uma professora uma vez nos disse uma frase que hoje faz todo o sentido: *"Nos tornamos um pedacinho de cada pessoa que amamos e passa no nosso caminho"*. E ao fim dessa jornada acadêmica de graduação eu tenho a certeza de que carrego um pedacinho de cada um que convivi. Minha família que me incentiva desde criança a seguir meus objetivos e proporcionam meios pra me apoiar. Os amigos que me acompanham desde o dia que sai em prantos da vitrine das profissões decidida a fazer farmácia. Os amigos que a universidade me permitiu conhecer e passar a amar. O grupo de pesquisa TECFARMA que foi minha segunda casa durante a graduação. Os professores, que tem tanto amor no que fazem e nos inspiram a estudar pra compartilhar conhecimento com o mesmo brilho nos olhos. Em especial a minha orientadora, que muito antes de me orientar oficialmente no TCC já era minha "ori" de vida e me ensinava tantas coisas, e hoje tenho muito orgulho de ter me tornado um pedacinho dela. Agradeço a cada uma dessas pessoas incríveis que me marcaram e me permitiram carregar um pedacinho de si mesmas para que eu pudesse crescer e me tornar farmacêutica.

APRESENTAÇÃO

O projeto intitulado "**Desenvolvimento de um pó hemostático à base de polissacarídeos e aminoácidos para controle de hemorragias**", submetido e aprovado na disciplina de TCC I do curso de Farmácia, pelo Comitê de Ética desta instituição, sob o Parecer 4.226.402 será apresentado na forma de artigo científico, como permite a disciplina de TCC II do curso de Farmácia. Em anexo, constam as instruções para os autores (Anexo 1) da Revista Carbohydrate Polymers, escolhida para a submissão do artigo.

Atenciosamente,



Fernanda Mendes de Moraes

Karine Modolon Zepon

Desenvolvimento de um pó hemostático à base de polissacarídeos e aminoácidos para controle de hemorragias

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Declaração de interesse: nenhuma

Resumo: Esse estudo desenvolveu um material hemostático na forma de pó associando os polissacarídeos *iota*-carragenana (ιC) e xiloglucana (XIL), o aminoácido L-serina (SER) e o fármaco ácido tranexâmico (ATX). O material foi produzido por liofilização seguida de maceração dinâmica e os materiais obtidos caracterizados por espectroscopia no infravermelho com transformada de Fourier (FT-IR), microscopia eletrônica de varredura (MEV) e análise de intumescimento. A atividade hemolítica e tempo de coagulação do pó hemostático preparado nesse estudo também foi investigada *in vitro.* A compatibilidade química entre os polissacarídeos, aminoácido e ATX foi confirmada nas análises de FT-IR. As imagens obtidas por MEV mostraram que o pó produzido apresenta uma superfície rugosa. A eficácia do pó hemostático foi determinada através da atividade hemolítica e tempo de coagulação *in vitro*,

demonstrando boa compatibilidade sanguínea e reduzindo pela metade o tempo de coagulação de um indivíduo saudável, indicando promissora capacidade no manejo do quadro hemorrágico, podendo contribuir para redução de mortes de pacientes.

Palavras-chave: ácido tranexâmico, *iota*-carragenana, xiloglucana, serina, pó hemostático.

1. Introdução

O quadro hemorrágico não controlado é uma das principais causas de morte potencialmente evitável entre pacientes, chegando a ser responsável por até 40% das mortes decorrentes de trauma, uma vez que um terço desses pacientes acabam não resistindo ao trajeto do local do acidente até o hospital (Altıntop et al., 2020; Curry et al., 2011). Hemorragias podem ser igualmente agravadas pelo uso de certos tipos de medicamentos e alguns tipos de condições congênitas (Hickman et al., 2018).

O manejo da hemorragia em ambiente hospitalar envolve principalmente o uso de suturas e eletro-cauterização (Barba et al., 2018). Em contrapartida, o controle hemorrágico em pacientes que não estão em ambiente hospitalar faz-se comumente pela compressão do local lesionado. No entanto, a eficiência da compressão na contenção hemorrágica é bastante limitada em lesões em locais de junção como virilha, pélvis, axilas, entre outros (Barba et al., 2018; Shen et al., 2020).

Com isso, como alternativa as modalidades de controle hemorrágicos tradicionais, diversos materiais hemostáticos para uso tópico têm sido propostos (Carvalho & Marchi, 2013). Um material hemostático ideal deve preencher algumas características que incluem, porém não se limitam à, promover rápida coagulação, possuir mínima reatividade tecidual, ter baixo custo e ser biocompatível (Kaur et al., 2013). Esponjas como o Hemospon®, microesferas como o

Arista™ AH e Celox™ e hidrogéis como Gel-Stop™ são alguns dos diversos tipos de materiais hemostáticos comercializados atualmente com indicação de uso tópico (Pereira et al., 2018; Su et al., 2019).

O mecanismo de ação de materiais hemostáticos tópicos envolve basicamente a concentração de fatores de coagulação por meio da absorção de fluidos, a selagem do sangue por mucoadesão e a atuação como pró-coagulante com participação direta na cascata da coagulação (Carvalho & Marchi, 2013). Deste modo, é comum que os materiais hemostáticos recentemente desenvolvidos combinem dois ou mais mecanismos de hemostasia visando melhorar sua performance (Shen et al., 2020).

Cientes disso, esse estudo desenvolveu um material hemostático na forma de pó associando materiais com mecanismos distintos de hemostasia. Logo, os polissacarídeos *iota*-carragenana e xiloglucana, o aminoácido L-serina e o ingrediente ativo farmacêutico ácido tranexâmico foram selecionados para esse estudo. Embora isoladamente alguns desses materiais já tenham sido investigados como agentes hemostáticos, no melhor do conhecimento dos autores não há estudos que reportem o uso combinado da ιC, XIL, SER e ATX na preparação de um material hemostático na forma de pó.

Ao que concerne a escolha dos polissacarídeos, estudos apontam que a grande capacidade de absorver água, ou seja, de intumescer, facilita a absorção da porção líquida do sangue acelerando dessa forma a ativação dos mecanismos endógenos de coagulação (Carvalho & Marchi, 2013; Xi et al., 2018). Sabendo que a inibição da fibrinólise é crucial no controle hemorrágico duradouro, a escolha de agentes antifibrinolíticos como o ATX faz-se essencial para impedir a dissolução da matriz de fibrina evitando que a lesão volte a sangrar (Altıntop et al., 2020). O uso tópico do ATX tem se mostrado eficiente na redução de sangramentos pós-operatórios e na diminuição da necessidade de transfusão de sangue sem causar complicações aos pacientes, tais avanços acabaram tornando-o reconhecido como fármaco essencial pela

Organização Mundial da Saúde (Chang et al., 2014; Hosseini et al., 2014; Zhang et al., 2019). Finalmente, a SER foi selecionada visando acelerar o processo de proliferação celular necessário para que ocorra a cicatrização da lesão (De Koning et al., 2003).

2. Metodologia

2.1 Materiais

O ácido tranexâmico (ATX) utilizado nesse estudo foi adquirido na Blau Farmacêutica (São Paulo, Brasil). A serina (SER) e o cloreto de cálcio foram adquiridos na LabSynth (São Paulo, Brasil). A *iota*-carragenana (ιC) foi cedida pela Extractos Naturales Gelymar S.A. (Santiago, Chile) e a xiloglucana (XIL) foi doada pelo Centre de recherches sur les macromolécules végétales (CERMAV, França).

2.2 Métodos

2.2.1 Preparação do pó liofilizado

Para a preparação do pó liofilizado, 0,5% de ιC ($^{m}/_{v}$), 0,5% de XIL ($^{m}/_{v}$) e 0,5% de SER ($^{m}/_{v}$) foram pesados e dissolvidos em água purificada e em seguida adicionado 1% ($^{m}/_{v}$) (amostra codificada como ιC:XIL:SER:ATX-1%) ou 2% ($^{m}/_{v}$) (amostra codificada ιC:XIL:SER:ATX-2%) de ATX. As soluções foram aquecidas até ~70°C em agitação constante por cerca de 30 min. Após a completa homogeneização, as soluções foram acondicionadas em placas de Petri e congeladas a –20°C durante 24 horas para posterior liofilização (liofilizador Terroni, Brasil). As amostras obtidas foram moídas via maceração dinâmica, em seguida submetidas ao processo de tamisação e armazenadas em dessecador (Fig. 1).

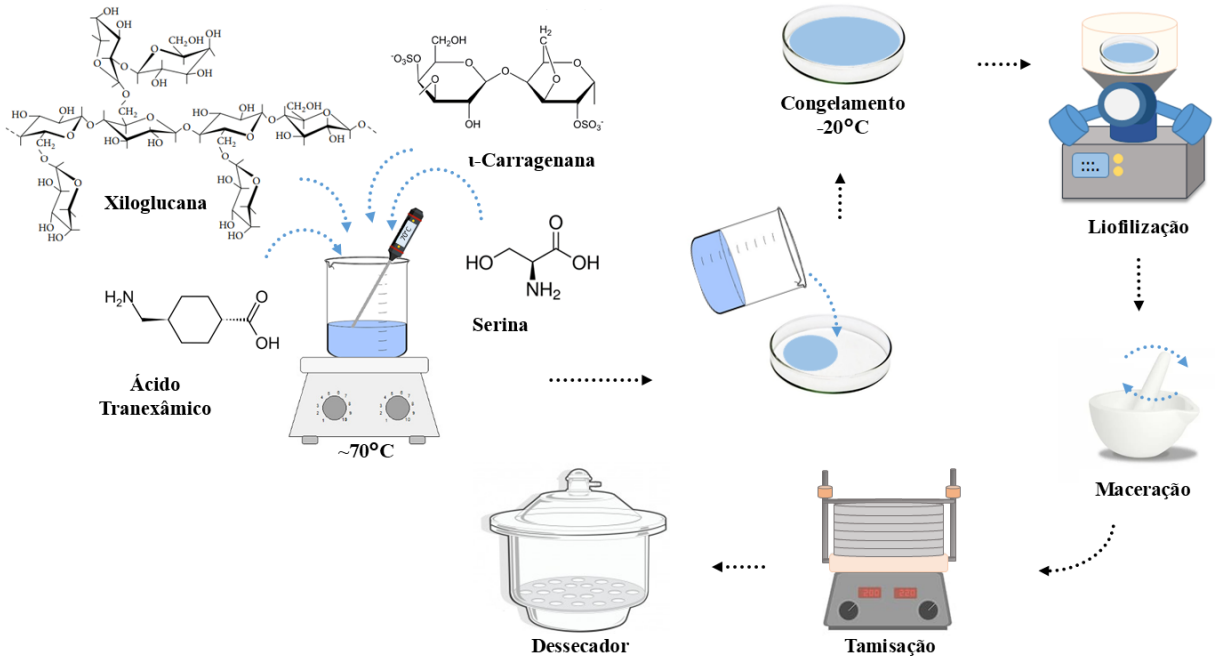

Fig. 1 Esquema detalhando o método de produção do pó liofilizado

2.3 Caracterização do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%

2.3.1 Morfologia da superfície

A caracterização morfológica do pó liofilizado foi feita via microscopia eletrônica de varredura usando o microscópio JEOL JSM-6510 com uma voltagem de aceleração de 10 kV. O pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% foi depositado sobre uma fita adesiva de carbono e então revestido com uma fina camada de ouro usando um *sputtering* à vácuo.

2.3.2 Espectroscopia no infravermelho com transformada de Fourier (FTIR)

A ocorrência de interações químicas entre os componentes foi avaliada no espectrofotômetro de absorção no infravermelho com transformada de Fourier IR PRESTIGE-2 (PerkinElmer, EUA), equipado com acessório de reflectância total. Os espectros de FT-IR de

XIL, ιC, SER e ATX assim como do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% foram obtidas na faixa de 4000 a 400 cm^{-1} com resolução de 4 cm^{-1}.

2.3.3 Intumescimento

A capacidade de intumescimento (S_w) do pó liofilizado foi realizada gravimetricamente (em solução tampão fosfato pH 7,4). Após determinada quantidade da amostra seca do pó liofilizado (w_0) foi colocada em um funil recoberto com papel filtro previamente umedecido com solução tampão fosfato. Em seguida, a solução de tampão foi lentamente gotejada sobre o pó liofilizado até a primeira gota escorrer do funil. A amostras saturadas foram então pesadas (w_s) para determinação da capacidade de intumescimento (S_w=[(w_s - w_0)/ w_0] *x* 100). Para determinação da perda de massa (w_l), as amostras submetidas a análise de intumescimento foram mantidas em estufa a 60°C até peso constante e pesadas (w_d). A perda de massa foi então determinada (w_l = [(w_o – w_d)/ w_d] *x* 100).

2.3.4 Coagulação *in vitro*

O efeito da quantidade do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% sobre a coagulação do sangue foi investigado usando sangue venoso coletado de doadores saudáveis em tubos contendo citrato de sódio 3,2%, seguindo as normas estabelecidas e aprovadas pelo Comitê de Ética em Pesquisa (CEP) da Universidade do Sul de Santa Catarina (parecer: 4.226.402). Amostras com 10, 20 ou 30 mg de pó liofilizado foram colocados em microtubos e então foi adicionado 500 µL de sangue e 25 µL de cloreto de cálcio (0,2 mol L^{-1}). Em tempos pré-determinados os microtubos foram homogeneizados até que o sangue perdesse a fluidez e ocorresse a formação de coágulos. Como controle negativo foi usado sangue recalcificado sem tratamento adicional (XI *et al*., 2018; BARBA *et al.*, 2018).

142 2.3.5 Hemólise *in vitro*

143 O teste de hemólise foi realizado visando determinar a compatibilidade sanguínea do pó
144 liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%. Amostras de 5 mL
145 de sangue venoso coletado em tubo contendo citrato de sódio 3,2% foram inicialmente diluídas
146 em 10 mL de solução salina 0,9%. Em seguida, 1,5 mL dessa solução foi adicionada em tubos
147 de ensaio contendo 30 mg do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e
148 ιC:XIL:SER:ATX-2% e mantidos em banho termostatizado (temperatura 37 ± 0,5°C) por 60
149 min. Após esse tempo, os tubos de ensaio foram centrifugados (1500 rpm) por 5 min sendo o
150 sobrenadante coletado e analisado em espectrofotômetro UV-vis (LGS 53, Bel Photonics,
151 Brazil) no comprimento de onda de 540 nm (Pan et al., 2017; Su et al., 2019). Água purificada
152 e solução salina 0,9% foram usadas como controle positivo e negativo, respectivamente, e a
153 taxa de hemólise foi então calculada pela equação abaixo:

154 $$\text{Taxa de hemólise (\%)} = \left(\frac{\text{absorbância}_{\text{amostra}} - \text{absorbância}_{\text{salina}}}{\text{absorbância}_{\text{água}} - \text{absorbância}_{\text{salina}}}\right) \times 100$$

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157 **3. Resultados e discussão**

158

159 O uso de polissacarídeos isoladamente ou em combinação com outros agentes
160 hemostáticos têm se apresentado como uma efetiva alternativa substitutiva para os materiais ou
161 métodos hemostáticos tradicionalmente usados no controle hemorrágico (Barba et al., 2018;
162 Biranje et al., 2020; Fathi et al., 2018; Punyanitya et al., 2019). Portanto, esse estudo
163 desenvolveu um material na forma de pó e à base polímeros naturais ιC e XIL aminoácido SER
164 e ATX sendo o ingrediente farmacêutico ativo destinado ao controle de hemorragias, visando
165 aplicação como agente hemostático de uso tópico. Na Fig. 2 pode ser verificada a aparência das
166 amostras liofilizadas, do pó obtido a partir da maceração dinâmica das amostras liofilizadas e

as micrografias obtidas por MEV do pó de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%.

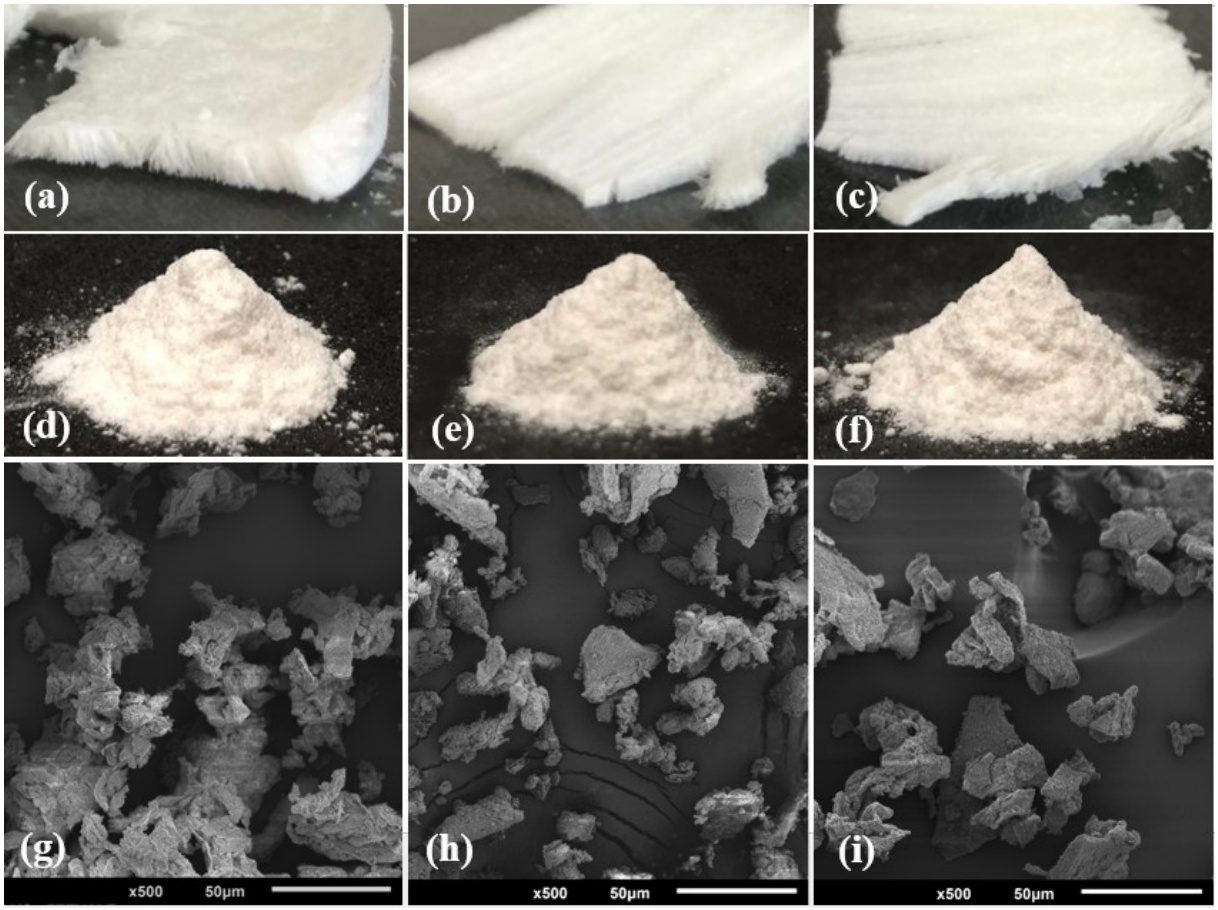
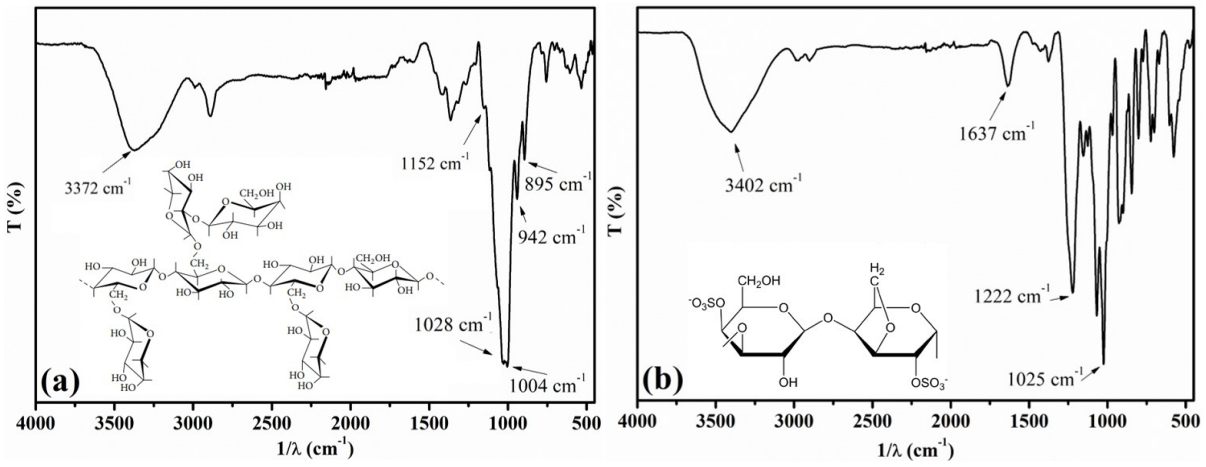


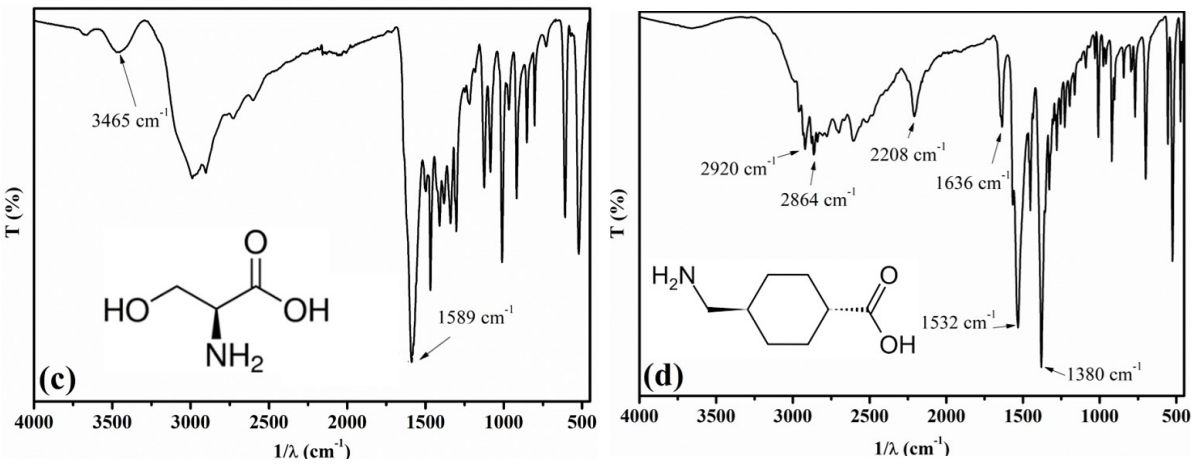
Fig. 2. Aparência da amostra liofilizada de ιC:XIL:SER (a), ιC:XIL:SER:ATX-1% (b) e ιC:XIL:SER:ATX-2% (c). Aparência do pó obtido a partir da maceração dinâmica da amostra liofilizada de ιC:XIL:SER (d), ιC:XIL:SER:ATX-1% (e) e ιC:XIL:SER:ATX-2% (f). Micrografias obtidas por MEV do pó de ιC:XIL:SER (g), ιC:XIL:SER:ATX-1% (h) e ιC:XIL:SER:ATX-2% (i).

O processo de liofilização das amostras ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% resultou na formação de um material com aparência esponjosa, homogêneo e de cor branca (Fig. 2a-c). A maceração dinâmica desses materiais levou a obtenção de um pó branco homogêneo com tamanho de partícula entre 250–100 µm (Fig. 2d-f).

Como observado nas micrografias de MEV (Fig. 2g-i), para as amostras de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%, o pó liofilizado apresentou uma superfície rugosa e com formato de partícula irregular. Notavelmente, partículas com formato irregular tendem a possuir uma maior área de superfície o que, para um material hemostático, é vantajoso considerando que essa característica acaba por favorecer a interação entre o material e o sangue, levando ao seu rápido intumescimento com subsequente formação do coágulo (Altıntop et al., 2020; Su et al., 2019).

Para uma melhor compreensão das possíveis interações entre os materiais que compõem o pó hemostático desenvolvido, na Fig. 3 tem-se os espectros de FT-IR de XIL, ιC, SER e ATX isolados e das amostras do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%.





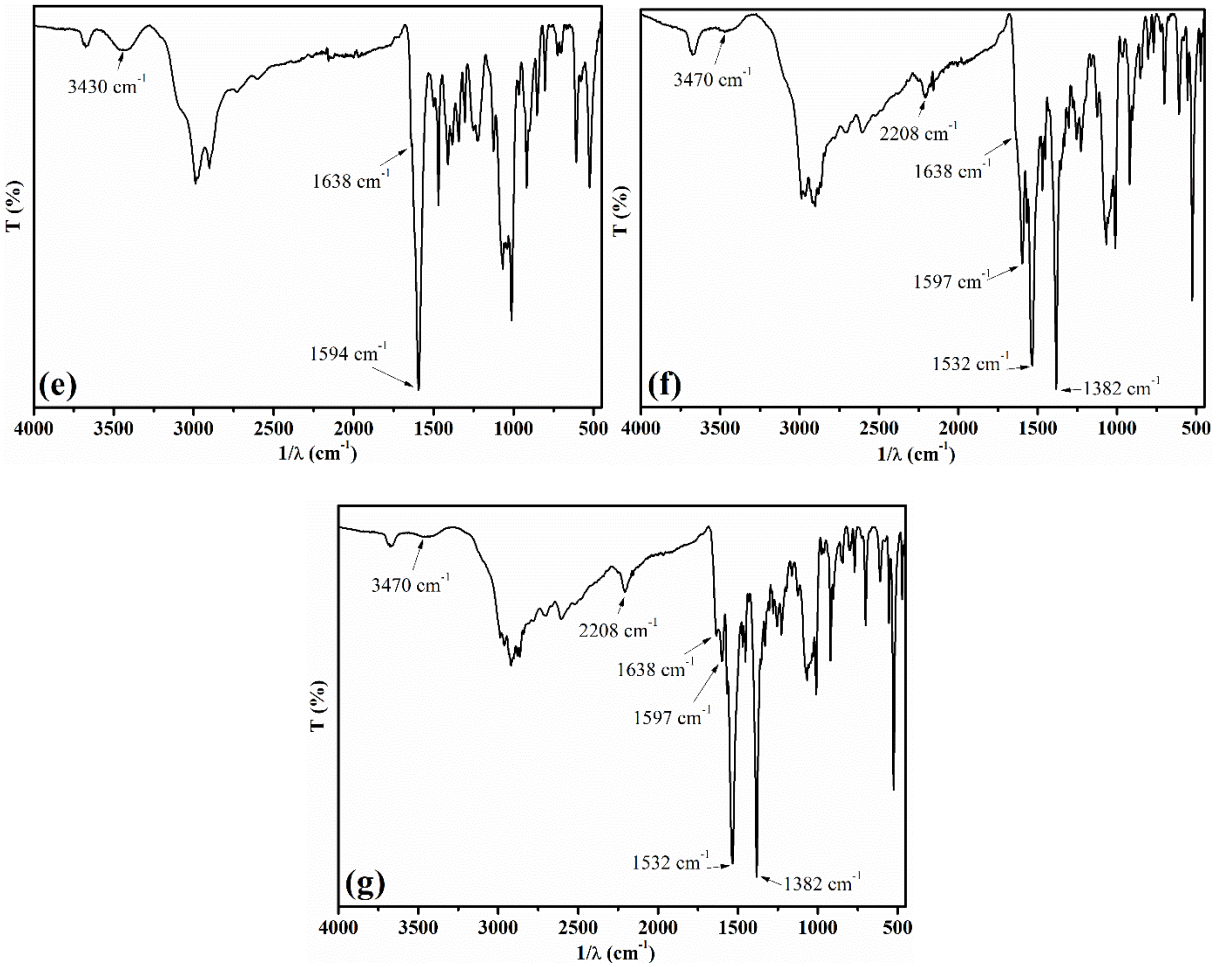


Fig. 3. Espectros obtidos por FT-IR para xiloglucana (a), *iota*-carragenana (b), serina (c), ácido tranexâmico (d), ιC:XIL:SER (e), ιC:XIL:SER:ATX-1% (f) e ιC:XIL:SER:ATX-2% (g).

O espectro de absorção da XIL (Fig. 3a) exibiu banda forte, larga (3600 e 3000 cm^{-1}), resultante da associação polimérica em decorrência das hidroxilas, com pico máximo de absorção em 3272 cm^{-1}, associada à deformação axial dos grupos ν(OH) (SANTOS et al., 2019). O espectro também revela diversas bandas de absorção entre 1200 e 850 cm^{-1} que surgem dos diferentes modos de vibração dos anéis de açúcares, no caso, glicose, xilose e galactose (Szymanska-Chargot & Zdunek, 2013). Destacando-se as deformações axiais e angulares C-O de diferentes éteres alifáticos em 1152, 1028 e 1004 cm^{-1}. O espectro da ιC (Fig. 3b) mostra uma ampla banda de absorção centrada em 3402 cm^{-1} atribuída a deformação axial dos grupos ν(OH), bandas de absorção em 1222 e 1025 cm^{-1} associadas à deformação dos grupos

ν(O=S=O) e dos grupos ν(C–O–C) que compõem a estrutura das unidades de galactose presentes na ιC (Ghani et al., 2019). A banda de absorção em 1637 cm^{-1} surge da deformação angular dos grupos δ(OH) de moléculas residuais de água presentes no polissacarídeo (Croitoru et al., 2020). Para o espectro da SER (Fig. 3b), uma banda de absorção atribuída à deformação axial dos grupos ν(NH_2) pode ser observada em 3465 cm^{-1}, banda larga em 2.960 - 2.850 cm^{-1} vibrações de deformação axial nos átomos de hidrogênio ligados a carbono, sobreposta a banda da ligação de hidrogênio intramolecular de OH com C=O. O espectro também revelou a presença de uma banda de absorção em 1589 cm^{-1} associada à deformação axial assimétrica dos grupos ν(COO^-) presentes na estrutura química da SER (Lambie et al., 2004). O espectro do ATX (Fig. 3d) exibiu banda larga de 3000 a 2200 cm^{-1} de intensidade moderada de vibrações de deformação axial nos átomos de hidrogênio ligados a carbono, oxigênio e nitrogênio (C-H, O-H e N-H), onde OH e NH associados a ligações diméricas ou poliméricas, e os picos 2920 e 2864 cm^{-1} relacionadas à deformação axial simétrica e assimétrica dos grupos ν(CH_2), respectivamente. A absorção na região 2200 cm^{-1} é associada às vibrações de deformação axial de deformações angulares de N-H e –NH_2. As bandas de absorção em 1636 e 1532 cm^{-1} atribuídas à deformação axial dos grupos ν(C=O) e a deformação angular dos grupos δ(NH_2), respectivamente. No espectro também foi possível observar bandas de absorção em 1380 cm^{-1} associada à deformação axial simétrica dos grupos ν(COO^-) (Shaikh et al., 2015).

O espectro FTIR da amostra ιC:XIL:SER (Fig. 3e) apresentou as bandas de absorção típicas da ιC, XIL e SER; comparado aos espectros dos materiais puros, a principal diferença no espectro da ιC:XIL:SER reside no descolamento da banda de absorção dos grupos ν(OH) para menor número de onda. Esse deslocamento pode estar relacionado à redução de grupos OH livres devido à formação de novas ligações de hidrogênio entre ιC, XIL e SER (Robert M. Silverstein, Francis X. Webster, n.d.). Ao comparar os espectros de ιC:XIL:SER (Fig. 3e) com os espectros de ιC:XIL:SER:ATX-1% (Fig. 3f) e ιC:XIL:SER:ATX-2% (Fig. 3g), as principais

diferenças são observadas na região de 2200 cm^{-1}, e entre 1600 cm^{-1} e 1300 cm^{-1}. As formulações ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%, apresentaram banda de absorção característica às vibrações de deformação axial de deformações angulares de N-H e -NH2 do ácido tranexâmico em 2200 cm^{-1}. O surgimento dos picos em 1535 cm^{-1} e 1383 cm^{-1}, característicos do ATX, confirmam sua inserção à formulação (Muthu & Prabhakaran, 2014; Shaikh et al., 2015). A absorção dos grupos ν(OH) para menor número de onda (3470 cm-1) também foi evidenciada nestas formulações semelhante espectro da ιC:XIL:SER.

A capacidade de um material hemostático em absorver líquidos é um dos mecanismos associados à sua ação no controle hemorrágico (Pan et al., 2017). Portanto, a capacidade de intumescimento do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% foi determinada usando uma solução tampão fosfato pH 7,4 (mimetizando o pH fisiológico). A amostra de ιC:XIL:SER absorveu 10,3 g de solução tampão pH 7,4 por grama da amostra em pó, enquanto as amostras ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% foram capazes de absorver 6,6 g e 6,2 g de solução tampão pH 7,4 por grama da amostra em pó, respectivamente. Essa redução na capacidade de intumescimento das amostras após adição do ATX pode estar relacionada à redução dos grupos -OH livres, conforme mostrou a análise por FT-IR. Embora a presença de ATX tenha reduzido a capacidade de intumescimento da matriz de ιC:XIL:SER, os valores de intumescimento foram próximos àqueles reportados em estudos prévios de SU e colaboradores (2019), onde micropartículas contendo diferentes concentrações de ATX (1% e 2%) apresentaram intumescimento médio 3,5 vezes menor daquele observado em nosso estudo, estando a redução da capacidade de intumescimento igualmente condicionada ao aumento da concentração de ATX.

Minimizar a lixiviação dos materiais que compõem o agente hemostático para a corrente sanguínea é essencial para mitigar possíveis efeitos tóxicos do produto. Portanto, a perda de massa do pó de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% após teste de

intumescimento foram 5,26% ± 2,82%, 7,5 % ± 1,45% e 12,66% ± 1,41%, respectivamente. Como podemos observar, há uma tendência de aumento da perda de massa do pó preparado com o aumento da quantidade de ATX presente na matriz. Considerando a natureza hidrofílica do ATX e sua baixa massa molar (157,21 g mol^{-1}), este resultado indica que o aumento da perda de massa observado com o aumento na concentração de ATX pode estar relacionado à sua lixiviação da matriz.

A tendência de intumescimento refletiu a análise de coagulação, que avaliou o período necessário para o sangue perder a fluidez e formar coágulos. Nas análises de 20 mg mL^{-1} e 40 mg mL^{-1}, os pós liofilizados de ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% apresentaram efeito limitado na formação do coágulo, quando comparadas à formulação ιC:XIL:SER , isenta de ATX. Contudo, na concentração de 60 mg mL^{-1} as três formulações se comportaram de forma semelhante, sendo capazes de coagular todo o conteúdo sanguíneo em 5 minutos (Fig. 4a).

O controle com sangue recalcificado atingiu completa coagulação após 10 minutos e as amostras tratadas com 60 mg mL^{-1} do pó liofilizado de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% induziram a coagulação em 30 segundos. Essa redução no tempo de coagulação pode estar associada à combinação de dois fatores: primeiro, a notável capacidade do pó preparado em absorver água – componente majoritário do sangue, conforme mostrou a análise de intumescimento; segundo, a atividade antifibrinolítica do ATX que resulta no retardo da fibrinólise, ou seja, a dissolução do coágulo (Hickman et al., 2018; Taam et al., 2020).

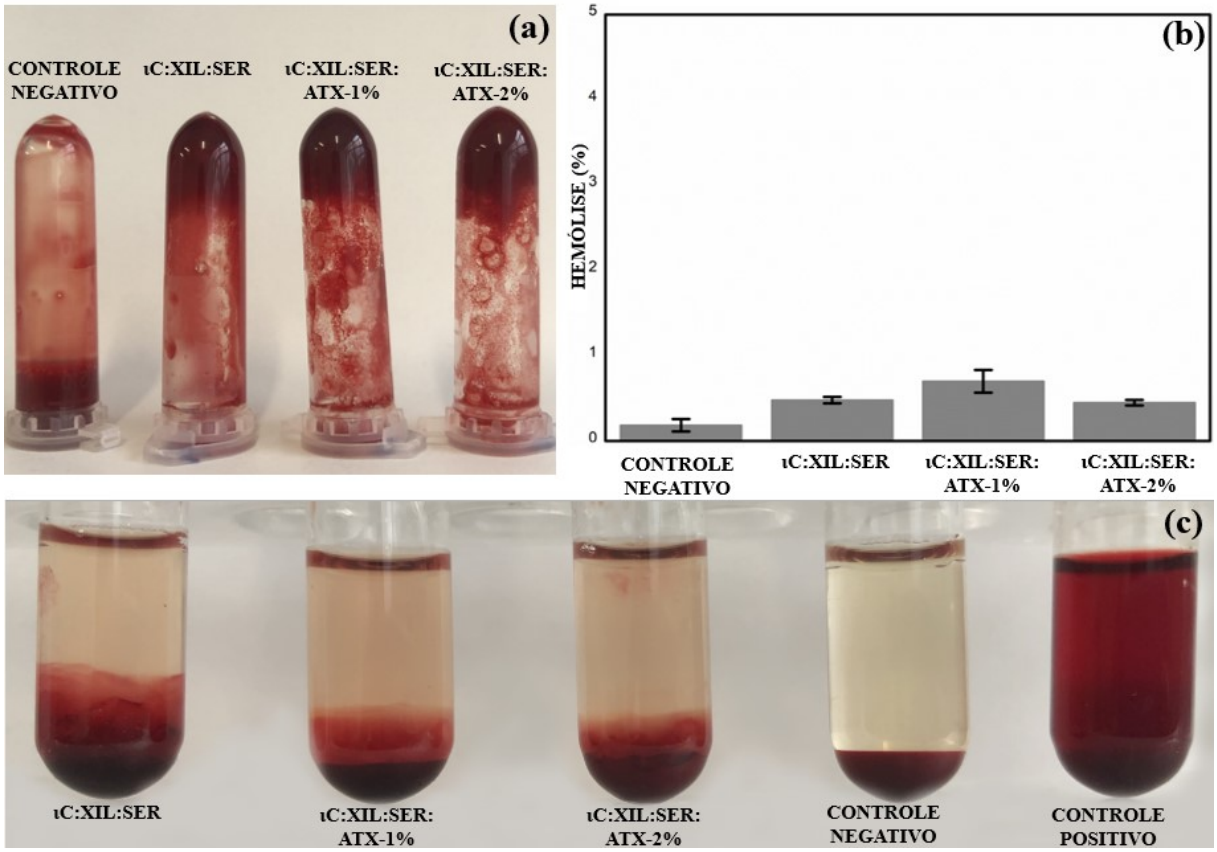


Fig. 4. Coagulação do sangue recalcificado (controle negativo) e sangue recalcificado tratado com 60 mg mL^{-1} do pó liofilizado após 5 minutos (a). Taxa de hemólise do sangue tratado com 60 mg mL^{-1} do pó liofilizado e controle negativo (sangue + salina 0,9%) (b). Atividade hemolítica do sangue tratado com 60 mg mL^{-1} do pó liofilizado (c).

A compatibilidade sanguínea das amostras de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% foi investigada através da atividade hemolítica e dissociação de hemoglobina. Como pode ser observado na Fig. 4c, o sobrenadante das soluções sangue/salina expostas as amostras preparadas nesse estudo apresentaram aspecto límpido similar ao controle negativo. Para que um material seja considerado biocompatível é estabelecido um limite máximo de 5% de hemólise (Su et al., 2019). Os valores de taxa de hemólise das amostras de ιC:XIL:SER, ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2% foram iguais a 0,484% ± 0,038%, 0,702% ± 0,131% e 0,482% ± 0,033%, respectivamente (Fig. 4b), confirmando a compatibilidade sanguínea do material hemostático preparado nesse estudo.

4. Conclusão

Os resultados apresentados nesse estudo revelaram o potencial de aplicação do material hemostático no manejo de hemorragias em diferentes cenários. A forma irregular das partículas do pó preparado combinada à inerente característica hidrofílica dos polissacarídeos e a atividade antifibrinolítica do ATX contribuíram para a notável atividade coagulante das amostras ιC:XIL:SER:ATX-1% e ιC:XIL:SER:ATX-2%. Ademais, a hemocompatibilidade das amostras preparadas nesse estudo sustenta seu caráter promissor.

Agradecimentos

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ANEXO 1 - INSTRUÇÃO AOS AUTORES

CARBOHYDRATE POLYMERS

A Journal Devoted to Scientific and Technological Aspects of Industrially Relevant Polysaccharides

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TABLE OF CONTENTS

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The role of the well-characterized carbohydrate polymer must be the major proportion of the work reported, not a peripheral topic. At least one named carbohydrate polymer must be cited and be the main focus of the paper and its title. Research must be innovative and advance scientific knowledge.

Characterization - For all polysaccharides, including those obtained from a supplier, essential structural information which will affect their behavior in the subsequent work should be given, along with a description of how that information was ascertained. Examples of such essential information include molecular weight, mannuronate/guluronate ratio for alginates, degree of esterification for pectin, degree of deacetylation for chitosan. Editors are unlikely to send papers for formal review with a statement such as "sodium alginate was purchased from XXX Inc." unless additional information is supplied. For papers involving synthesis, polysaccharide derivatives must also be wellcharacterized. For papers describing identity or application of newly-discovered polysaccharides, purity and monosaccharide composition are essential; some molecular size and linkage information is highly desirable.

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- biosynthesis
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- polyalkanoates, polylactic acid, or lignin
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- routine studies of complexation of a drug with a single cyclodextrin
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- production and isolation of enzymes which act on polysaccharides (studies on the mode of action of an enzyme on a polysaccharide are within the journal scope)
- carbohydrate oligomers where the degree of polymerization is less than four
- treatments of cotton fabrics and cellulose-based paper where the research is largely not about the component cellulose itself
- use of carbohydrate polymers as a support material (e.g. in enzyme immobilization, chromatography, etc.) where there is no specific involvement of the chemistry of the carbohydrate polymer.

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