3D-PRINTED BIOADHESIVE ORAL PATCH FOR LONG-ACTING NALTREXONE DELIVERY

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Introduction

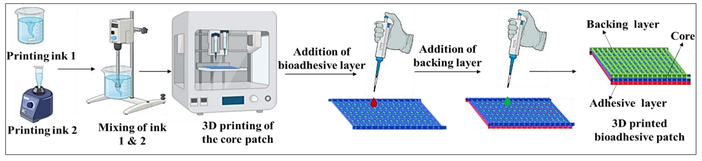
Chronic conditions such as hypothyroidism, alcohol addiction, and diabetes require long-term medication, with the oral route being preferred for its convenience and patient compliance. However, conventional oral drug delivery systems often necessitate frequent dosing due to inadequate residence time in the gastrointestinal tract. The objective of the present study is to develop a 3D printed bioadhesive gastric patch for long-acting naltrexone hydrochloride (NTX) delivery. The gastric patch is designed to adhere to the gastric mucosa and release NTX for more than 30 days to improve therapeutic efficacy and patient adherence.

Objectives

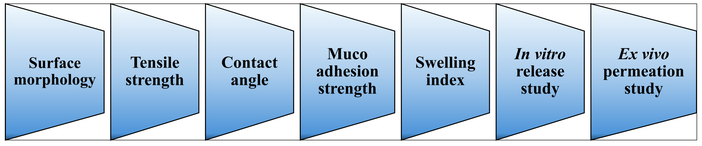
- The aim of this study was to fabricate and characterize a 3D printed (3DP) bioinspired long-acting bioadhesive gastric patch to deliver NTX through oral route.
- To evaluate the localization, pharmacokinetics and safety of the 3DP patches in Sprague Dawley rats after oral administration .

Methodology

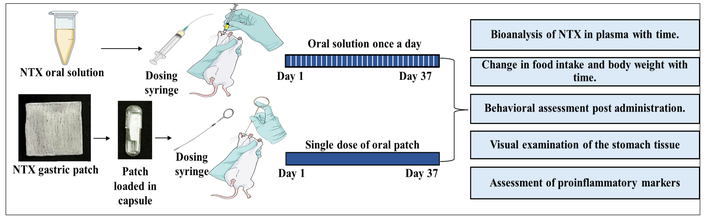
➢ Fabrication of NTX loaded 3D printed patch



➢ Characterization of 3D printed NTX patch



➢ *In vivo* evaluation of 3D printed NTX patch



Results and Discussion

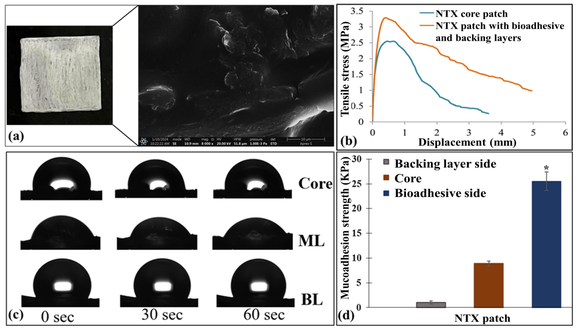


Figure 1. (a). Representative digital image of 3DP patch, scanning electron microscopy of mucoadhesive layer, **(b).** Tensile stress vs Displacement curves of the patches, **(c).** Representative contact angle of core patch, backing layer (BL) and mucoadhesive layer (ML), **(d).** Mucoadhesion strength after adhering to mucosal side of the excised rat stomach, Asterisk (*) represents that values are significantly different at $P < 0.05$. Data represents mean ± standard deviation, where n = 4.

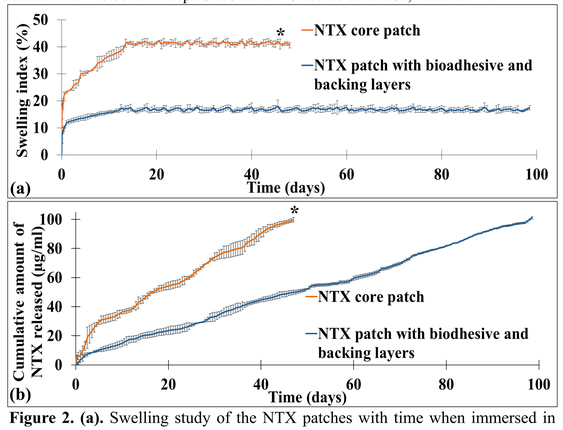


Figure 2. (a). Swelling study of the NTX patches with time when immersed in simulated gastric fluid (SGF). **(b).** *In vitro* release of NTX from patch in SGF. Data represents mean ± standard deviation, where n = 4. Asterisk (*) represents that values are significantly different at $P < 0.05$.

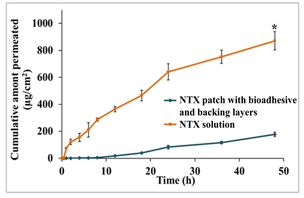


Figure 3. *Ex vivo* permeation study of NTX from 3DP patch and solution through the excised rat stomach tissue.

Table 1. ***Ex vivo*** **permeation parameters**

Ex vivo parameters	NTX patch	NTX solution
Flux (µg/cm²/h)	3.5 ± 0.4*	72.8± 13.5
Lag time (h)	6.7 ± 0.4*	0.2 ± 0.08
Permeability coefficient ($x10^{-3}$cm²/h)	3.3 ± 0.37	4.1 ± 0.8

Data represents mean ± standard deviation, n=3.* represents that values are significantly different at $P < 0.05$.

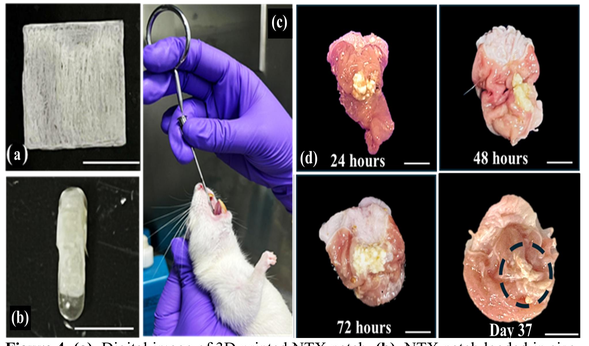


Figure 4. (a). Digital image of 3D printed NTX patch, **(b).** NTX patch loaded in size 9 capsule, **(c).** Oral administration of NTX capsule in Sprague Dawley rat, **(d).** Localization of NTX gastric patch in body region of stomach at 24, 48, 72h and 37 days post oral administration. Scale on (a), (b) and (d) represents 1cm, 4.2mm, and 7mm, respectively.

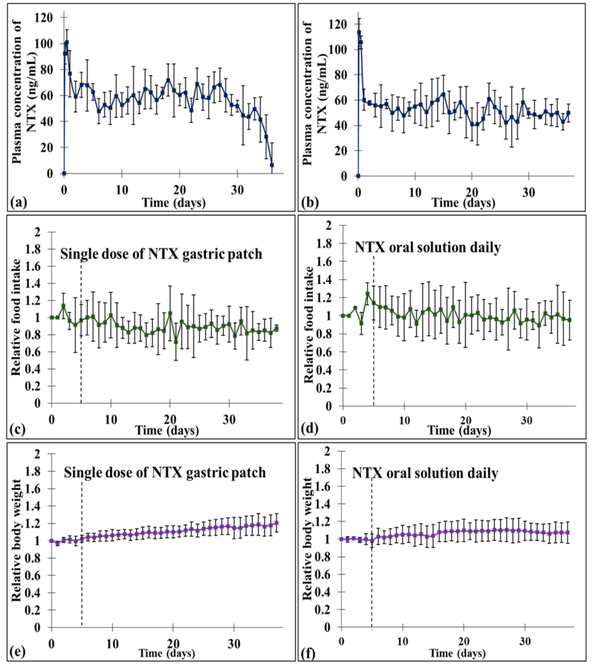


Figure 5. *Invivo* pharmacokinetic studies. Plasma concentration of NTX after administering **(a).** Oral patch, **(b).** Oral solution in SD rats. Body weight and food intake changes in rats administered with **(c,e)** oral patch, **(d,f)** oral solution. Data represent mean ± standard deviation, where n = 6.

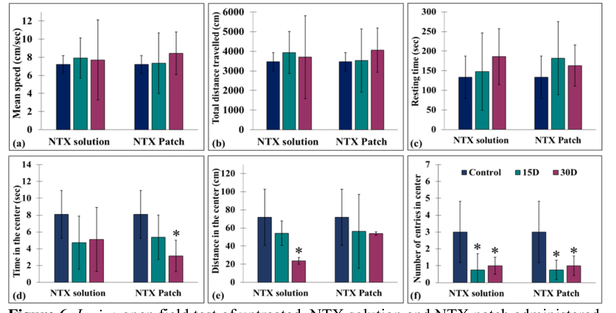


Figure 6. *Invivo* open field test of untreated, NTX solution and NTX patch administered animals to monitor **(a,b,c).** Locomotor activities i.e. mean speed, total distance travelled, resting speed, and **(d,e,f,).** Anxiety parameters i.e. time in center, distance in center and number of entries in center, Data represent mean ± standard deviation, where n = 6. Asterisk (*) represents that the values are significantly different compared to control at $P < 0.05$.

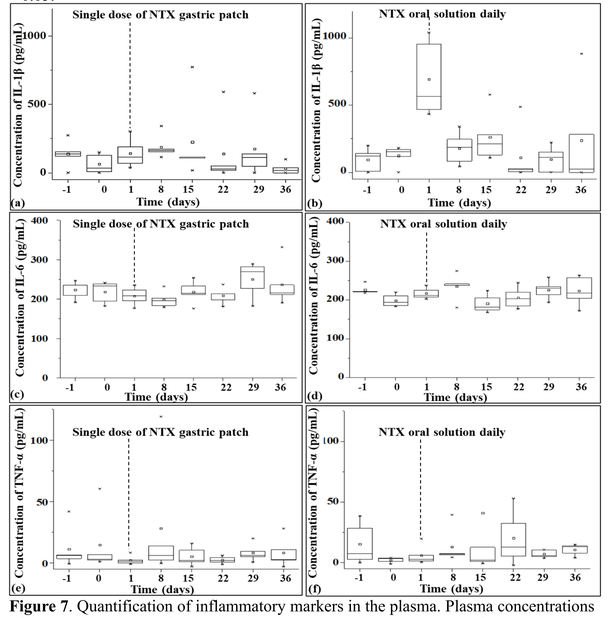


Figure 7. Quantification of inflammatory markers in the plasma. Plasma concentrations of interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) after administration of NTX patch **(a,c,e),** NTX oral solution **(b,d,f)**, respectively. Data represents mean ± standard deviation, where n=6.

Conclusion

The oral administration of 3D printed bioinspired mucoadhesive gastric patch showed sustained plasma concentration of 42 to 69 ng/mL of NTX for upto 37 days.

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