FINECELL'S CELLULOSE HYDROGEL

Description

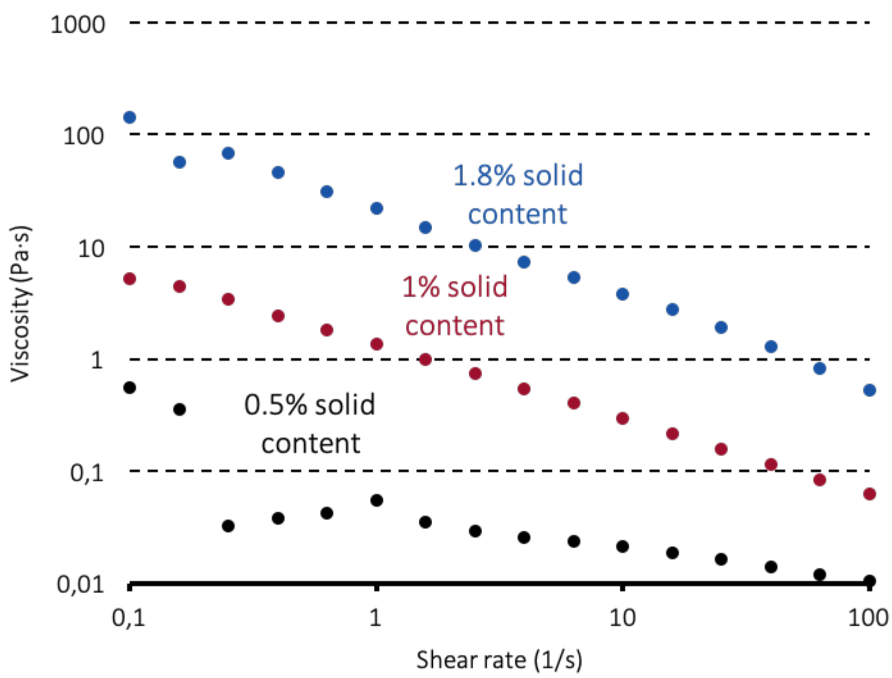
FineCell's Cellulose Hydrogel is a thick and shear thinning suspension of cellulose microfibers in water.

- pH≈7
- Usually delivered at a solid content of 2.5%
- Translucent and odorless
- Storage at 4°C, shelf life up to one year

Viscosity and rheology

The cellulose microfibers in our hydrogel form a continuous, strong, and stable gel network with excellent shape forming ability. Therefore, adding our cellulose hydrogel into bioink formulations will significantly improve the shape fidelity of the printed scaffolds. Our cellulose hydrogel is also shear thinning. When shears (e.g. the pressure during printing) are applied, the viscosity of the hydrogel drops quickly, which makes the hydrogel flow easily. By removing the applied shears, the viscosity of the hydrogel recovers quickly, which is the key for a quick formation of the desired shape. See the viscosity of our cellulose hydrogel at different solid content and shear rate in the table and figure below:

Shear rate (1/s)	Viscosity at 1.8% solid content (Pa·s)	Viscosity at 1% solid content (Pa·s)	Viscosity at 0.5% solid content (Pa·s)
0.1	141.8	5.2	0.5
1	22.0	1.4	0.05
10	3.8	0.3	0.02



Shear thinning is an important property for achieving great printability at moderate printing pressure. It's also important for the cell's survival upon printing cell-laden bioinks, as the cells would become distorted and broken at too high printing pressure.

Biocompatibility

FineCell's Cellulose Hydrogel is non-toxic towards living cells and has excellent biocompatibility.

Cell viability	Cell line	Test method
99%	Mammal fibroblasts BALB/3T3 clone A31	Cytotoxicity, Direct contact test ISO 10993-5:2009
95%	Mammal fibroblasts BALB/3T3 clone A31	Cytotoxicity, Elution test ISO 10993-5:2009

Find test reports below:
Direct contact test:
http://finecell.se/wp-content/uploads/2019/10/227df398-e2a0-4c46-bd15-cca3ba0cd387.pdf
Elution test:
http://finecell.se/wp-content/uploads/2019/10/3aa57730-823a-4864-87eb-edd9a599bb92.pdf

Printing parameters

FineCell's Cellulose Hydrogel can be printed at the following conditions:

Temperature	Room temperature
Printing rate	5 mm/s
Nozzle size	25 G (inner diameter 0.25 mm)
Pressure	20-60 kPa

Crosslinking

Thanks to its unique surface functionality, FineCell's Cellulose Hydrogel is crosslinkable with $CaCl_2$ during printing. In this way, the printed scaffolds can maintain their structural integrity. To further improve their stability, post-print crosslinking may be applied, such as impregnation with 1,4-butanediol diglycidyl ether (BDDE) at 50°C for 2h [1]. UV crosslinking with the help of a photoinitiator in the bioink formulation is also applicable.

FORMULATING WITH OTHER BIOPOLYMERS

Hydrogels solely consisting of water suspensions of cellulose microfibers can be used as monocomponent bioinks for printing scaffolds that support cell adhesion and proliferation [1]. However, it is recommended to mix FineCell's Cellulose Hydrogel with another biopolymer such as alginate, GelMA, gelatin, and hyaluronic acid, to achieve optimal cell adhesion and proliferation.

Dilution of FineCell's Cellulose Hydrogel

FineCell's Cellulose Hydrogel is usually delivered at a solid content of 2.5%. For formulating bioinks, the recommended solid content of the cellulose microfibers in the final formulation is 1-2%. It is also recommended to dilute the cellulose hydrogel to the desired solid content early in the formulating process, by taking the total amount of water in the final formulation into consideration. The dilution is preferably done by using a high-shear mixer, such as an Ultra Turrax at 15000 RPM for 5 min, but more gentle mixing techniques may also be used, provided that a longer mixing time is allowed.

Bioink's formulation and application

FineCell's Cellulose Hydrogel can be formulated together with a wide range of bio-based polymers such as alginate, gelatin, GelMA, and hyaluronic acid, to make bioinks with optimal cell adhesion and proliferation.

Bioink composition	Content of cellulose	Content of other biopolymers	Printing rate; nozzle size; pressure	Crosslinking condition	Biocompatibility according to literature	Ref.
Cellulose + Alginate	2%	0.5%	10-20 mm/s; 0.3 mm; 20-60 kPa	90 mM $CaCl_2$; 10 min	Human chondrocyte cells; viability 73% (day 1), 86% (day 7)	[2]
	2%	0.5%	5 mm/s; 0.15 mm; 40 kPa	100 mM $CaCl_2$; 10 min	Human and rabbit chondrocyte cells; viability 96% (human), 99% (rabbit)	[3]
	1.36%	0.5%	0.26 or 0.41 mm; 6-28 kPa	100 mM $CaCl_2$; 12 min	Bovine chondrocyte cells; viability >85% (day 14), >88% (day 28)	[4]
	1.8%	1.2%	10-20 mm/s; 0.3 mm; 20-30 kPa	100 mM $CaCl_2$; 5 min	Human pluripotent stem cells; good proliferation at day 5	[5]
Cellulose + GelMA	1%	0.2% or 0.5%	2000 mm/min (33 mm/s); 0.15 mm (30 G); 65-70 kPa	0.5% Irgacure 2959; 10 mW/cm^2 UV (365 nm); 5 min	Mouse fibroblast cells; viability >90%	[6]
Cellulose + Gelatin	2%	6%	5-15 mm/s; 0.21 mm and 0.41 mm; 160 kPa	20°C; 6 h	Mouse fibroblast cells; good proliferation (no significant difference when comparing with the control) at day 7	[7]
Cellulose + Hyaluronic acid	3%	1.29%	17 kPa	0.001% H_2O_2; 5 min	Mouse mesenchymal stem cells; viability 95% (Day 7)	[8]

Mixing with Cells

For making cell-laden bioinks, we recommend mixing the bioinks with a high concentration (10-30 million cells per ml of bioink) of cells. Mixing can be done through either gentle agitation (e.g. mixing manually with a spatula), or co-extrusion of the bioinks and cell suspensions into one syringe cartridge, which can then be loaded on a bioprinter. It's important to avoid air bubbles in the mixture, as they will affect the printability of the cell-laden bioinks.

References

1. Xu, C.; Molino, B.Z.; Wang, X.; Cheng, F.; Xu, W.; Molino, P.; Bacher, M.; Su, D.; Rosenau, T.; Willför, S.; et al. 3D printing of nanocellulose hydrogel scaffolds with tunable mechanical strength towards wound healing application. J. Mater. Chem. B 2018, 6, 7066-7075.

2. Markstedt, K.; Mantas, A.; Tournier, I.; Martínez Ávila, H.; Hägg, D.; Gatenholm, P. 3D bioprinting human chondrocytes with nanocellulose-alginate bioink for cartilage tissue engineering applications. Biomacromolecules 2015, 16, 1489-1496.
3. Ávila, H.M.; Schwarz, S.; Rotter, N.; Gatenholm, P. 3D bioprinting of human chondrocyte-laden nanocellulose hydrogels for patient-specific auricular cartilage regeneration. Bioprinting 2016, 1-2, 22-35.
4. Müller, M.; Öztürk, E.; Arlov, Ø.; Gatenholm, P.; Zenobi-Wong, M. Alginate sulfate-nanocellulose bioinks for cartilage bioprinting applications. Ann. Biomed. Eng. 2017, 45, 210-223.
5. Nguyen, D.; Hägg, D.A.; Forsman, A.; Ekholm, J.; Nimkingratana, P.; Brantsing, C.; Kalogeropoulos, T.; Zaunz, S.; Concaro, S.; Brittberg, M.; et al. Cartilage tissue engineering by the 3D bioprinting of iPS cells in a nanocellulose/alginate bioink. Sci. Rep. 2017, 7, 658.
6. Xu, W.; Molino, B.Z.; Cheng, F.; Molino, P.J.; Yue, Z.; Su, D.; Wang, X.; Willför, S.; Xu, C.; Wallace, G.G. On low-concentration inks formulated by nanocellulose assisted with gelatin methacrylate (GelMA) for 3D printing toward wound healing application. ACS Appl. Mater. Interfaces 2019, 11, 8838-8848.
7. Xu, X.; Zhou, J.; Jiang, Y.; Zhang, Q.; Shi, H.; Liu, D. 3D printing process of oxidized nanocellulose and gelatin scaffold. J. Biomater. Sci. Polym. Ed. 2018, 29, 1498-1513.
8. Henriksson, I.; Gatenholm, P.; Hägg, D.A. Increased lipid accumulation and adipogenic gene expression of adipocytes in 3D bioprinted nanocellulose scaffolds. Biofabrication 2017, 9, 015022.