Brazilian Journal of Experimental Design, Data Analysis and Inferential Statistics

Federal University of Rio de Janeiro

BJEDIS, Rio de Janeiro, Special Edition, v. 01, 2021, Page:40

DOI: https://doi.org/10.55747/bjedis.v1i1.48405

E-ISSN: 2763-6925

Special Edition **Received 01/27/2021. Revised 01/29/2021. Accepted 02/05/2021. Published 05/13/2021.**

Drug delivery polymers: An Analysis Based on Literature Text Mining

Emiliane Daher*[1], Fernando Gomes[1,2], Jean Carelo[1], and Viviane Brandão[1]

[1]Instituto de Macromoléculas Professora Eloisa Mano, Centro de Tecnologia-Cidade Universitária, av. Horacio Macedo, 2030, bloco J. Universidade Federal de Rio de Janeiro, Brazil,; [2] Programa de Engenharia da Nanotecnologia, COPPE, Centro de Tecnologia-Cidade Universitária, av. Horacio Macedo, 2030, bloco I. Universidade Federal de Rio de Janeiro, Brazil.

Abstract: Many polymers are used as drug carriers for controlled delivery because of its many advantages. To find the most used polymers for this purpose in recent years, we chose to use Text Mining as an evaluation tool. Text Mining tool was precious in this work to identify the main polymers that contributed to drug delivery, allowing us to draw a map year by year based on correlation analyzes. Firstly, an analysis was made on what was most researched per year, and then what were the most cited polymers. Then the most mentioned polymers were separated and organized to observe which year it was more or less cited. It was found with this work that none of the polymers showed only positive correlations in all years. Besides, polymers did not reveal individual growth in their use over the years. The Text Mining presented here proved to be an efficient and quick way to observe the desired theme and open up possibilities for research in different fields.

Keywords: Text mining; Polymer; Drug delivery; Biodegradable; Biocompatible, Data mining.

Adherence to the BJEDIS' scope: The article is in agreement with the scope since it is a literature review using the data mining tool.

*Instituto de Macromoléculas Professora Eloisa Mano, Centro de Tecnologia - Cidade Universitária, Av. Horacio Macedo, 2030, bloco J. Universidade Federal de Rio de Janeiro, P.O. Box: 21941-598, Rio de Janeiro, Brazil; Tel: ++55-21-98238-9002, e-mail: emilianedaher@hotmail.com

1. INTRODUCTION

The kinetic control of drug release offers numerous advantages compared to traditional methods, including increased efficacy, reduced toxicity, and increased patient compliance with treatment (1–4). These delivery systems often use natural and synthetic polymers as carriers for drugs (5–8). An important consideration when polymers are used for this purpose is the destination of the polymer after the drug is released (9). Thus, polymers that are naturally excreted by the body, called biodegradable polymers, are desired (10, 11). They can be excreted directly via the kidney or can be metabolized into smaller molecules that will later be excreted. Many polymers are already used as drug carriers. Among these, there are natural polymers such as chitosan(12–14), alginate(15–17) and cellulose-based polymers(18–20), and biodegradable polyesters, such as poly (ε-caprolactone) – PCL (21–23), poly (lactic acid) – PLA (24, 25) and poly (lactic acid) co-glycolic) – PLGA (26–29). Image 1 shows the natural polymers chitosan, alginate and cellulose and Figure 2 the biodegradable polyesters PCL, PLA and PLGA.

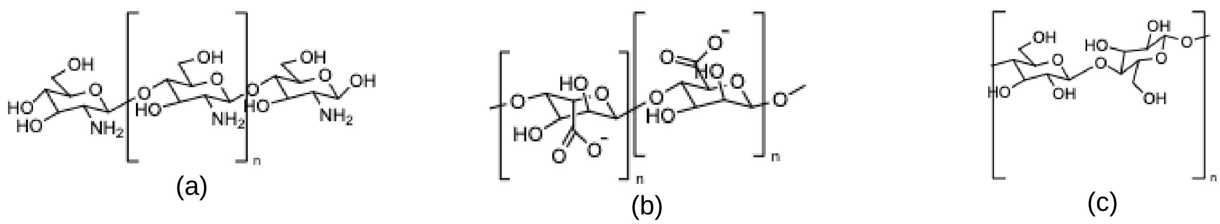

Figure 1. Molecules of (a) chitosan; (b) alginate; (c) cellulose

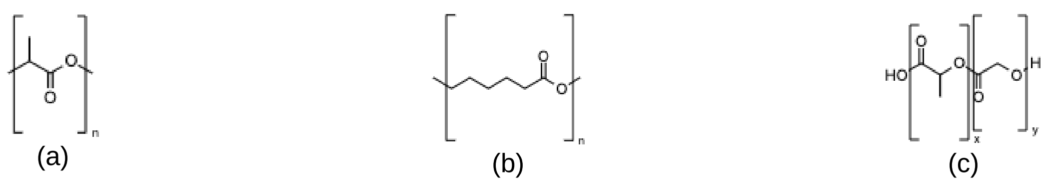

Figure 2. Molecules of (a) PLA; (b) PCL; (c) PLGA

Natural polymers are often used to produce microcapsules due to their advantages of biocompatibility and biodegradability (30, 31). Hydroxypropylmethylcellulose (HPMC) polymers are often studied for controlled release systems, as they are non-toxic and easy to handle (32). HPMC is a semi-synthetic ether derived from cellulose (33). The hydrophilic matrix tablets based on it offer several advantages in the development of a prolonged-release formulation orally, such as the flexibility of modulating the release, the simplicity of preparation, low production costs, and "Scaleup" facility (34). Besides, these polymers can be used to control the release of both water-soluble and insoluble drugs (35, 36). Poly (ε-caprolactone), PCL is a biodegradable polyester widely studied for drug release applications (37–39). PCL is a highly hydrophobic, semicrystalline aliphatic polymer that degrades very slowly "in vitro" and "in vivo" (40,41). As it has a high permeability to many drugs and has no toxicity, PCL is a very suitable polymer for controlled release of drugs (42). Biodegradable polylactides - PLA, homo, and copolymers have been widely studied as drug carriers. They show great potential as transport systems for increasing active molecules, as they do not cause adverse reactions to tissues. They also have excellent biocompatibility and controlled biodegradability property(43, 44).

As shown above, polymers are widely used in scientific research seeking the controlled release of drugs. Among these polymers, some are more used than others, due to their characteristics and advantages. To find out which polymers are most used for controlled drug delivery, text mining (45–47) was carried out. “Text mining can be broadly defined as a knowledge-intensive process in which a user interacts with a document collection over time by using a suite of analysis tools.”(48, 49)

2. METHODOLOGY

In this text mining, scientific articles containing the words “drug delivery” and "polymer" were collected using the ScienceDirect database (https://www.sciencedirect.com/) on may 25th, 2020. Ninety thousand eight hundred fifty-six results were retrieved from this database, allowing for observing an increase in the number of publications during studied years, as shown in Figure 3. Based on this search, the time was limited between 2009 and 2019, since the year 2020 was not completed, presenting a smaller number of papers.

The first 100 most relevant papers (filter option selected on ScienceDirect) of each year in the period from 2009 to 2019 were selected and collected totaling 1100 articles. These articles were separated into two topics according to each year: (i) title and (ii) abstract to facilitate analyzing the main words listed in the documents. The used tools were LibreOffice Calc and LibreOffice Writer (both version: 6.2.3.2 Build ID: aecc05fe267cc68dde00352a451aa867b3b546ac). The online tool used for Text Mining was Voyant Tools (https://voyant-tools.org/) (50–56). The set conditions were Fixed-term: "polymer" and Minimum coverage: 5%.

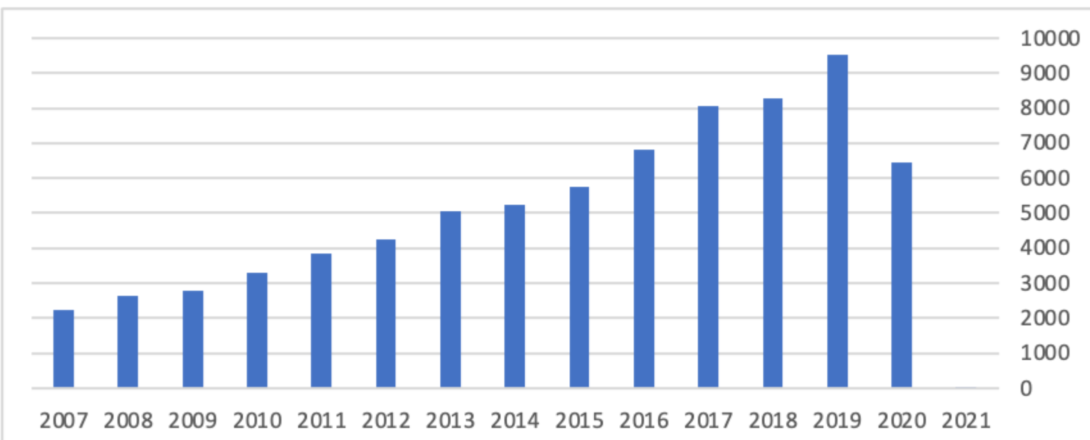

Figure 3. ScienceDirect search sorted by year

For the analysis, the data of the titles were placed on the Voyant, year by year. The correlation tool was used, and the term fixed was "polymer". The correlation and significance data were copied to an Excel spreadsheet from LibreOffice. The same procedure was followed for abstracts. The purpose of this analysis was to present a broad idea of what each year studied most. Besides, with the arrangement of words organized in order of more excellent correlation, it was possible to verify which polymers were most used. LibreOffice Calc search tool was used for this purpose. The names of the polymers were searched and marked year by year. To identify the names of the polymers, in addition to knowledge in the area, the correlations of the titles were used, since they had fewer words (around 100 words) than the abstracts.

3. DISCUSSION

One way to extract text data more naturally is by using the Text Mining technique. Text Mining has invaluable commercial value since it’s a simplified and faster way to collect data and can be applied in different areas (57–73).

A closer observation of each year in the studied period was relevant to understanding the roadmap that the subject has followed along these eleven years. Aiming to perform this complicated assignment, the Voyant’s Correlation tool (74,75) was used, and the most relevant, irrelevant, and non-related terms were listed year by year. Figure 4 and 5 shows a word cloud obtained using voyant from 2010 and 2017 titles file respectively.

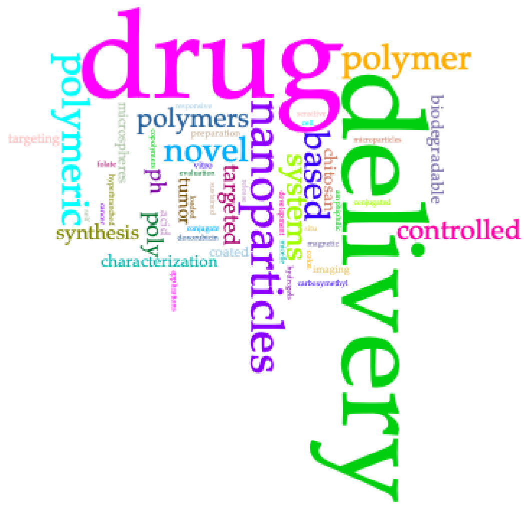

Figure 4. Word cloud extracted from voyant (2010)

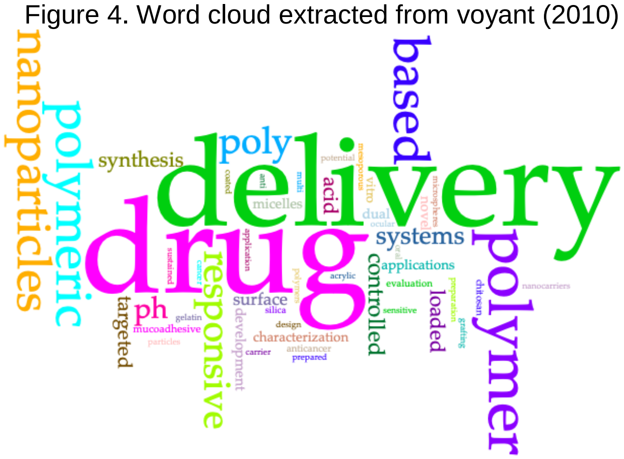

Figure 5. Word cloud extracted from voyant (2017)

It is possible to perform the calculation by comparing the relative frequencies of the exploited terms using Voyant's Correlation tool. However, to analyze the results, a piece of prior statistical knowledge is needed. When the correlation is close to zero indicates that the two words are not related. A positive correlation suggests that the two words move together. On the other hand, the negative correlation indicates that the two words move in opposite directions. In all cases, the relationship between the words becomes more reliable as correlation is closest to ± 1 (76–79). Another important information that can be extracted is the significance value (p). When p is lower than 0.05, indicates that, with more than 95% probability, the null hypothesis can be rejected, and the studied values are not randomly distributed (80–82). The Correlations tool allows exploring the extent to which the frequencies of terms vary in sync.

Table 1 shows the correlations between the polymer and the most relevant terms extracted in the search, using Voyant Tools, from the Titles and Abstracts. The words that have statistical relevance ($p < 0.05$) (83) were marked with asterisks, however it was only possible to extract the p values from the first 100 and last 100 words, which is why the tables are incomplete. The highest correlation values, regardless of whether their sign is positive or negative, were listed in Table 1. The non-related and most irrelevant term was also recorded. Besides, all of the generated Weblinks to Voyant Tools' corpus are listed in Table 2.

Table 1 - Correlations between polymer and 2nd terms in 2009-2019 Titles & Abstracts

Fixed term		Titles			Abstracts		
		2nd term	r	p	2nd term	r	p
Polymer	2009	cell*	0.6690	0.03441	like*	0.8981	0.00041
		controlled	-0.0236	0.94832	brust	-0.0074	---
		drug*	-0.6730	0.02393	allow*	-0.7295	0.01665
	2010	degradation	0.7727	0.00878	capability	0.8642	0.00125
		chitosan	-0.0141	0.9689	consisted	-0.0047	---
		conjugate	-0.7793	0.0078	attributed	-0.7394	0.0145
	2011	imaging	0.8427	0.022	micelles	0.9055	0.0003
		chitosan	-0.0171	0.9623	act	-0.0029	---
		diclofenac	-0.6698	0.0340	ir	0.7931	0.0061
	2012	Cell	0.6666	0.3526	cell	0.7906	0.0158
		delivery	-0.0581	0.8732	performance	-0.0022	----
		glycolic	-0.6546	0.0399	chloride	-0.8230	0.0034
	2013	Hybrid	0.6881	0.0278	microspheres	0.9372	0.0001
		Poly	-0.0421	0.9079	inflammation	-0.0016	----
		Film	-0.5976	0.0680	confocal	-0.7936	0.0061
	2014	effect*	0.6522	0.04098	area*	0.8262	0.0032
		nanoparticles	-0.0120	0.97381	cancer	-0,0012	---
		inulin*	-0.9875	0.02802	impact*	-0.7279	0.0170
	2015	nanoparticle*	0.7237	0.01797	nuclear*	0.8879	0.0006
		Anti	-0.0754	0.83604	led	-2.2E-8	---
		novel*	-0.6592	0.03813	addition*	-0.7769	0.0082
	2016	imprinted*	0.8040	0.00506	5.0*	0.7307	0.0164
		Acid	-0.0736	0.83995	caprolactone	-1.3E-8	---
		block	-0.5056	0.13596	particularly*	-0.7573	0.0112
	2017	optimization*	0.8487	0.00190	needles*	0.8460	0.0020
		assessment	-0.0223	0.95130	micellar	-1.3E-8	---
		imaging	-0.3694	0.29351	cell*	-0.8012	0.0053
	2018	gelatin*	0.8249	0.00331	day*	0.8625	0.0013
		brachytherapy	-0.0190	0.95853	degree	-3.1E-8	---
		Drug	-0.2844	0.42573	blood*	-0.7423	0.0139
	2019	improved*	0.7510	0.01229	capability*	0.8410	0.0023
		efficient	-0.0259	0.94339	characteristics	-1.6066	---
		liposome	-0.4154	0.23258	dose*	-0.7539	0.0118

* Statistically relevant terms

Table 2 – Weblinks to Voyant Tools' corpus

Year	Titles
2009	https://voyant-tools.org/?corpus=addcd175e457517b133cff5372c986c4
2010	https://voyant-tools.org/?corpus=3be6b49d069b7b61bf4d22ae7e38cde1
2011	https://voyant-tools.org/?corpus=661f5d5a722b2ee8998b567625ff5422
2012	https://voyant-tools.org/?corpus=c9b6d52409b332a1a4335f61dc0f3d27
2013	https://voyant-tools.org/?corpus=9e3385e84e5fcb043851cb42e7ca76aa
2014	https://voyant-tools.org/?corpus=9e176f171da754f36149c0d7ff24556a
2015	https://voyant-tools.org/?corpus=2f64b57058989e71d5982920b2cc5360
2016	https://voyant-tools.org/?corpus=734e563770ec987d156c2ea339146034
2017	https://voyant-tools.org/?corpus=da714676d7c833f2090b6bffb158377b
2018	https://voyant-tools.org/?corpus=e711ce509d2c5c80a3f563863a891d4a
2019	https://voyant-tools.org/?corpus=98c095ef43b28bf74723e711aad9c3ae

Year	Abstracts
2009	https://voyant-tools.org/?corpus=c59025cbe7f7e7a4df4e721df8ededcc
2010	https://voyant-tools.org/?corpus=d16490252154d995d2734ed0442d71b5
2011	https://voyant-tools.org/?corpus=b7d7ae341e9253b5e9fc5aeaba2b6a5e
2012	https://voyant-tools.org/?corpus=de257c4bed398ea85b8f7a4284444131
2013	https://voyant-tools.org/?corpus=3088f5db4b98d101e8f29a30f46fc3fe
2014	https://voyant-tools.org/?corpus=ef97b6dba62e14c176d3c59edd72a248
2015	https://voyant-tools.org/?corpus=02b07e6634d89ec9b2d2bb98d4da166d
2016	https://voyant-tools.org/?corpus=023f68ab26948afba9a26af276188c73
2017	https://voyant-tools.org/?corpus=eed9fe743e83115d982a076b0351cf19
2018	https://voyant-tools.org/?corpus=5a25b1d2ba84522b73bb8710530aabc3
2019	https://voyant-tools.org/?corpus=78dfe39d5ba9f7049df1d62a4d0c565b

In 2009, the main correlations in the titles with polymers were *cells* and *containing* and in abstracts *like* and *method*. These words do not tell much about what was being researched at this year. Among the polymers with a positive correlation in titles are PLA, chitosan, and PEG. With negative correlations are cellulose, PLGA, and PCL. Among the abstracts, the polymers that appear with positive correlations were: polyacrylamide, PLA, PEG, polymethacrylate, PEO, and PLGA. The polymers that appear with negative correlation are chitosan, cellulose, PCL, alginate, PEO, and polyacrylic.

During 2010, the main correlations in titles with polymers were *degradation* and *conjugated* and in abstracts *capability* and *gastric*. With these words, it is possible to have an idea about what was being researched this year, the data allows concluding that the polymers were used in addition to obtaining controlled release, to have a gastric protection, improving bioavailability of drugs. As was done by Hari et al. 2010 (84) and Chen et al. 2010 (5). Among the polymers with a positive correlation in the titles is only cellulose. With negative correlations were chitosan, polyacrylic, alginate PLGA, and PEG. In the abstracts, the polymers that appear with positive correlations were: carboxymethylcellulose, gelatin, PCL, alginate, PLA, PEO, PEG, chitosan, and polymethacrylate. The polymers that appear with negative correlation were dextran, PLGA, pluronic, and cellulose.

In 2011, the main correlations in titles with polymers were *imaging* and *carrier* and in abstracts *micelles* and *labile*. With these words, it is possible to have an idea that the research that year was focused on imaging exams and that for that, the polymer matrices carried some particle in the form of micelles. As was done by Wang et al. 2011(85) and Li et at. 2011(86). Among the polymers with a positive correlation in the titles are PEG, PLGA, acrylic, and carboxymethylcellulose. With negative correlations were chitosan, PEO, and PLA. In the abstracts, the polymers that appear with positive correlations were: PCL, pluronic, PEO, PMA, cellulose, PEG, and collagen. The polymers that appear with negative correlation were alginate, PLA, PEG, PLGA, PGA, and chitosan.

In 2012, the main correlations in titles with polymers were *cell* and *improved* and in abstracts *cell* and *inflammation*. With these words, It is possible to think that the research that year focused more on anti-inflammatory drugs. The research of Gulati et al. 2012, used the anti-inflammatory indomethacin (87) and the research of Machín et al. 2012 used naproxen (88). Among the polymers with a positive correlation in the titles is only the PLGA. Cellulose had a zero correlation, and with negative correlations were chitosan, PEG, algitane, PCL, polyacrylamide, and PLA. In the abstracts, the polymers that appear with positive correlations were: PEG, cellulose, polyacrylate, PLGA, PEO, dextran, PCL, PMA, pluronic, and PLA. The polymers that appear with a negative correlation were chitosan, polyacrylamide, and alginate.

In 2013, the main correlations in the titles with polymers were *hybrids* and *collagen* and abstract *microspheres* and *extrudates*. With these words, it is possible to have the idea that the research was more focused on hybrid polymers and formation of microspheres with these matrices for drug delivery, just as it was done by Gao et al. 2013 (89), Deng et al. 2013 (90, 91). This year, the macromolecule collagen, had great prominence and appeared among the most cited words. The polymers with a positive correlation were PEG and gelatin and with negative correlation were alginate, PCL, dextran, chitosan, methacrylate, and chitin. In the abstracts, the polymers with positive correlations were: color, PEG, PLGA, cellulose, gelatin, alginate, PLA, chitosan, and PCL. The polymers that appear with negative correlation were pluronic, polyacrylamide, chitin, PEO, PMA, polyglycerol, and dextran.

In 2014, the main correlations in titles with polymers were *effect* and *conjugates* and in abstracts *area* and *designed*. These words did not tell much about what was being researched at the time. Looking for the polymers that appear in these correlations, the only one that appears with a positive correlation in the titles was polyethylene glycol (PEG)—followed by PCL and chitosan, the latter two with negative correlations. In the abstracts, the polymers that appear with positive correlations, in order, were PLA, gelatin, poly(ethylene oxide) (PEO), PEG, PCL, and PLGA. Pluronic and acrylic polymers such as poly (methyl methacrylic) (PMMA) appear with a negative correlation this year and cellulose.

In 2015, the main correlations in the titles with polymers were *nanoparticle* and *MR imaging* and in the abstracts *nuclear* and *conjugate*. Observing these words is possible to conclude that the research was focused on the use of nanoparticles coated with polymers for imaging exams such as magnetic resonance (92), Ho et al. 2015 (93) and Huang et al. 2015 (94). The only polymer that appears with a positive correlation in the titles is chitosan and with negative correlation PEG and cellulose. In the abstracts, the polymers that appear with positive correlations, in order, were the acrylic polymethacrylate and polymethacrylic (PMA), PLA, PEO, the cellulose derivative carboxymethyl cellulose (CMC) and PLGA. The polymers that appear with negative correlation were PCL, gelatin, PEG, chitosan, and alginate.

In 2016, the main correlations in titles with polymers were *imprinted* and *microspheres* and in abstracts *novel* and *graffiting*. These words show that the research that year could be focused in molecularly imprinted polymers and the drugs were being inserted more and more into microspheres, to perhaps try to avoid the "burst" release. Hemmati et al. 2016 (95–97) used molecularly imprinted polymers in their research that year. The only polymer that appeared in the positive correlations of the titles was alginate. The PEG appeared with correlation equal to zero, and the polymers with negative correlations were chitosan, pluronic, and PEO. In the abstracts, the polymers that appear with positive correlations, in order, are chitosan, the acrylic polymer methacrylamide, mPEG, alginate, PMMA, and ethyl cellulose. The polymers that appear with negative correlation were PCL, PLA, PEO, and pluronic.

In 2017, the main correlations in the titles with polymers were *optimization* and *alkyl* and in *needless* and *evidenced*. These words did not tell much about what was being researched at the time.
The polymers that appear with a positive correlation in the titles were alginate and gelatin with a very high correlation equal to 0.64 and 0.44, respectively. With negative correlations were PEG and cellulose. In the abstracts, the polymers appear with positive correlations, in order, were: PLA, PEG, methacrylic, PCL and chitosan. The polymers that appear with negative correlations were alginate, gelatin, PCL, HPMC, PEO, PLGA, and cellulose.

In 2018, the main correlations in the titles with polymers were *gelatin* and *multifunctional* and in abstracts *novel* and *day.* These words did not tell much about what was being researched at the time. Among the polymers with a positive correlation in titles were, besides gelatin, PLA and PEG. With negative correlations were chitosan and PLGA. In the abstracts, the polymers that appear with positive correlations, in order, were: PLA, gelatin, polyglycerol, poly isopropyl acrylamide, and PLGA. The polymers with negative correlation were PCL, PEG, polycarbonate, PEO, alginate, chitosan, and cellulose.

In 2019, the main correlations in titles with polymers were *improved* and *intracellular* and in *capability* and *assemblies*. These words could show that the research was focused in self-assembling polymers. Bai et al. 2019 (98), Wang et al. 2019 (99) and Gao et al. 2019 (100) used self-assembling polymers in their research. Among the polymers with a positive correlation in the titles were alginate, pluronic, PEG, and PCL. With negative correlations were chitosan and PGA. In the abstracts, the polymers that appear with positive correlations were: PLA, PEG, polyacrylic, alginate, PLGA, and PCL. The polymers that appear with negative correlation were chitosan, CMC, pluronic, PEO, and PCL.

To have a better idea of how the polymers were used, a separation by polymer was made to follow which year that polymer was used more or less. For this, the most cited polymers were chosen and organized in a decreasing way according to the correlation taken from Voyant as shown in Table 3, using PEG as an example.

Table 3. Organization of PEG citations according to the correlation extracted from the voyant tool

PEG titles				PEG abstracts			
YEAR	POSITION	CORRELATION	P	YEAR	POSITION	CORRELATION	P
2013	8	0.5661	0.0880	2017	99	0.4861	0.1543
2011	13	0.5123	0.1301	2013	244	0.3070	---
2009	39	0.1821	0.6147	2019	264	0.3037	---
2018	36	0.1707	0.6373	2014	260	0.280	---
2019	35	0.1036	0.7758	2016	308	0.1836	---
2014	31	0.0937	0.7967	2012	485	0.1049	---
2016	60	0	1	2015	534	-0.0440	---
2017	94	-0.3563	0.3121	2018	638	-0.1088	---
2010	83	-0.36364	0.3016	2009	798	-0.1935	---
2015	88	-0.4277	0.2176	2011	840	-0.2126	---
2012	92	-0.4364	0.2073	2010	1143	-0.6083	0.0621

As can be seen, there has been no increase or decrease in PEG use over time, but a disorderly variation from year to year. It was concluded that PEG was more used for drug delivery in 2013 since it had a high positive correlation in titles and abstracts. It was less used in 2010 since it had high negative correlations both in titles and abstracts.

As in the case of PEG, the polymer alginate also had a disorderly variation from year to year. However, unlike PEG, this polymer does not appear in the titles in all the research years. According to the research, in 2019, alginate was the most used polymer for the controlled release of drugs, presenting high values of positive correlation in both titles and abstracts. The research also showed that 2012 was the year that least mentioned alginate since the correlations were negative, and this polymer was in the last place when ordering the years, both in titles and abstracts.

Chitosan had the same disorder profile through the years but with a peculiarity. This polymer had only two years with a positive correlation in the titles, 2009 and 2015, but these years showed negative correlations in the abstracts. Thus, it was not possible to know which year the most used chitosan for drug delivery. On the other hand, it was possible to observe the year that least cited this biopolymer for this purpose, which was 2014, since it presented high negative correlation values in both titles and abstracts.

Polycaprolactone (PCL), like alginate, does not appear in the titles in all the research years. Despite PCL presenting only one positive correlation in the titles in 2019, PLC had a more significant positive correlation in abstracts in 2011 (correlation equal to 0.6081 with p equal to 0.0622), which was much higher than the 2019 correlation in abstracts (equal to 0.0818), showing that this polymer was much more applied to drug delivery in 2011. The year that least used the PCL for this purpose, according to the research, was in 2009 as it presents higher values of negative correlations both in abstracts and in titles comparing with other years.

PLA, which was not cited in the titles every year researched (such as alginate and PCL), was the polymer with the highest number of positive correlations, having only negative correlations in the titles in 2011 and the abstracts in 2011 and 2016. Therefore, it was concluded with the research that the year that least used the PLA for this purpose was in 2011 since it had slightly higher values of negative correlation (equal to -0.1719). The year that PLA was most used was in 2018 (abstract correlation equal to 0.7015). In addition to this polymer having the highest positive correlation value, PLA presented four years with correlation values above or equal to 0.5 in the abstracts, which shows that this polymer deserves great prominence when it comes to controlled drug delivery.

As cellulose is used for controlled release in different forms (different derivatives) such as carboxymethylcellulose and hydroxyethylcellulose), the individual analysis of this polymer has been compromised. It is not shown in this work, despite being widely applied for this purpose.

The data obtained confirm that polymers such as Chitosan, PCL, PLGA, PEO, and Pluronic presented more significant positive correlations in the first years of the studied period. On the other hand, polymers such as alginate, acrylics, PEG, and PLA have the most considerable positive correlations in the last years of the research.

These correlation values allow forecasting that these last polymeric systems will be the most researched in the coming years. This growing interest in these materials is the result of greater control over the physical and chemical characteristics obtained from the synthesis of polymers. In other words, reproducibility will guide the choice of polymers in the coming years.

4. CONCLUSIONS

The Text Mining presented in this work proved to be an efficient, fast, and reliable way to observe the desired theme and opens up a range of possibilities for research in different fields. The study proved that the most used polymers for controlled drug delivery between 2009 -2019 were natural polymers such as alginate, chitosan, gelatin, chitin, and cellulose. In turn, among synthetic polymers, PEG, PCL, PLA, PLGA, pluronic, PEO, and some acrylic polymers such as polyacrylic were the most researched. However, none of the polymers showed only positive correlations in all years. Besides, polymers did not reveal individual growth in their use over the years, proving that they were researched without a primary material target focus in this period. Since polymers such as alginate, acrylics, PEG, and PLA have the most considerable positive correlations in the last years of the research, the correlation values allow forecasting that these polymeric systems will be the most researched in the coming years.

5. ACKNOWLEDGMENTS

Tthe authors thank Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES - -Finance Code 001), Financiadora de Estudos e Projetos (FINEP PRESAL Ref.1889/10) and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ).

REFERENCES

1. LI, Yan and LEE, Ping I. A new bioerodible system for sustained local drug delivery based on hydrolytically activated in situ macromolecular association. International **Journal of Pharmaceutics**. v. 383, n. 1, p. 45–52. 2010. DOI https://doi.org/10.1016/j.ijpharm.2009.09.005.

2. BUTUN, Sultan, INCE, Fatma Gul, ERDUGAN, Huseyin and SAHINER, Nurettin. One-step fabrication of biocompatible carboxymethyl cellulose polymeric particles for drug delivery systems**. Carbohydrate Polymers**. v. 86, n. 2, p. 636–643. 2011. DOI 10.1016/j.carbpol.2011.05.001.

3. PAUN, Irina Alexandra, MOLDOVAN, Antoniu, LUCULESCU, Catalin Romeo and DINESCU, Maria. Biocompatible polymeric implants for controlled drug delivery produced by MAPLE**. Applied Surface Science**. v. 257, n. 24, p. 10780–10788. 2011. DOI 10.1016/j.apsusc.2011.07.097.

4. DUWA, Ramesh, EMAMI, Fakhrossadat, LEE, Sooyeun, JEONG, Jee-Heon and YOOK, Simmyung. Polymeric and lipid-based drug delivery systems for treatment of glioblastoma multiforme**. Journal of Industrial and Engineering Chemistry**. v. 79, p. 261–273. 2019. DOI 10.1016/j.jiec.2019.06.050.

5. LIU, Changhua, CHEN, Yanqing and CHEN, Jianguang. Synthesis and characteristics of pH-sensitive semi-interpenetrating polymer network hydrogels based on konjac glucomannan and poly(aspartic acid) for in vitro drug delivery**. Carbohydrate Polymers**. v. 79, n. 3, p. 500–506. 2010. DOI 10.1016/j.carbpol.2009.08.024.

6. RATTANAKIT, Parawee, MOULTON, Simon E., SANTIAGO, Karen S., LIAWRUANGRATH, Saisunee and WALLACE, Gordon G. Extrusion printed polymer structures: A facile and versatile approach to tailored drug delivery platforms**. International Journal of Pharmaceutics**. v. 422, n. 1, p. 254–263. 2012. DOI 10.1016/j.ijpharm.2011.11.007.

7. ASADI, Ebadullah, ABDOUSS, Majid, LEBLANC, Roger M., EZZATI, Noushin, WILSON, James N. and KORDESTANI, Davood. Synthesis, characterization and in vivo drug delivery study of a biodegradable nano-structured molecularly imprinted polymer based on cross-linker of fructose**. Polymer**. v. 97, p. 226–237. 2016. DOI 10.1016/j.polymer.2016.05.031.

8. HATANAKA, Tomomi, SAITO, Takanori, FUKUSHIMA, Takaaki, TODO, Hiroaki, SUGIBAYASHI, Kenji, UMEHARA, Soichi, TAKEUCHI, Tomoharu and OKAMURA, Yosuke. Potential of biocompatible polymeric ultra-thin films, nanosheets, as topical and transdermal drug delivery devices**. International Journal of Pharmaceutics**. v. 565, p. 41–49. 2019. DOI 10.1016/j.ijpharm.2019.04.059.

9. WANG, Sujun, LUO, Yanfeng, ZHOU, Jin, WANG, Mingxing and WANG, Yuanliang. PLA-PEG-FA NPs for drug delivery system: Evaluation of carrier micro-structure, degradation and size-cell proliferation relationship**. Materials Science and Engineering: C**. v. 91, p. 297–302. 2018. DOI 10.1016/j.msec.2018.05.049.

10. LIU, Ying, JIANG, Zifei, HOU, Xuefeng, XIE, Xingmei, SHI, Jiangpei, SHEN, Junyi, HE, Yuanzhi, WANG, Zhi and FENG, Nianping. Functional lipid polymeric nanoparticles for oral drug delivery: Rapid mucus penetration and improved cell entry and cellular transport**. Nanomedicine: Nanotechnology, Biology and Medicine**. v. 21, p. 102075. 2019. DOI 10.1016/j.nano.2019.102075.

11. MUHAMAD, Ida [Idayu. Revolutionizing Therapeutic Drug Delivery: Intelligent Polymeric Systems and Hybrid Nano-carriers**. Materials Today: Proceedings**. v. 5, p. S149–S153. 2018. DOI 10.1016/j.matpr.2018.08.057.

12. FERRARI, Priscileila C., OLIVEIRA, Giselle F., CHIBEBE, Flávia Cristina S. and EVANGELISTA, Raul C. In vitro characterization of coevaporates containing chitosan for colonic drug delivery**. Carbohydrate Polymers**. v. 78, n. 3, p. 557–563. 2009. DOI 10.1016/j.carbpol.2009.05.021.

13. LIU, Li, TANG, Ximin, WANG, Yuanyuan and GUO, Shengrong. Smart gelation of chitosan solution in the presence of NaHCO3 for injectable drug delivery system**. International Journal of Pharmaceutics**. v. 414, n. 1, p. 6–15. 2011. DOI 10.1016/j.ijpharm.2011.04.052.

14. POURJAVADI, Ali, TEHRANI, Zahra [Mazaheri and JOKAR, Safura. Chitosan based supramolecular polypseudorotaxane as a pH-responsive polymer and their hybridization with mesoporous silica-coated magnetic graphene oxide for triggered anticancer drug delivery**. Polymer**. v. 76, p. 52–61. 2015. DOI 10.1016/j.polymer.2015.08.050.

15. VASILE, Cornelia, DUMITRIU, Raluca Petronela, CHEABURU, Catalina Natalia and OPREA, Ana Maria. Architecture and composition influence on the properties of some smart polymeric materials designed as matrices in drug delivery systems. A comparative study**. Applied Surface Science**. v. 256, n. 3, Supplement, p. S65–S71. 2009. DOI 10.1016/j.apsusc.2009.04.120.

16. KULKARNI, Raghavendra V., BOPPANA, Rashmi, MOHAN, G. [Krishna, MUTALIK, Srinivas and KALYANE, Navanath V. pH-responsive interpenetrating network hydrogel beads of poly(acrylamide)-g-carrageenan and sodium alginate for intestinal targeted drug delivery: Synthesis, in vitro and in vivo evaluation**. Journal of Colloid and Interface Science**. v. 367, n. 1, p. 509–517. 2012. DOI 10.1016/j.jcis.2011.10.025.

17. ATHAMNEH, Tamara, AMIN, Adil, BENKE, Edit, AMBRUS, Rita, LEOPOLD, Claudia S., GURIKOV, Pavel and SMIRNOVA, Irina. Alginate and hybrid alginate-hyaluronic acid aerogel microspheres as potential carrier for pulmonary drug delivery**. The Journal of Supercritical Fluids**. v. 150, p. 49–55. 2019. DOI 10.1016/j.supflu.2019.04.013.

18. BUILDERS, Philip F., IBEKWE, Nneka, OKPAKO, Larry C., ATTAMA, Anthony A. and KUNLE, Olobayo O. Preparation and characterization of mucinated cellulose microparticles for therapeutic and drug delivery purposes**. European Journal of Pharmaceutics and Biopharmaceutics**. v. 72, n. 1, p. 34–41. 2009. DOI 10.1016/j.ejpb.2008.12.011.

19. MATHARU, Amol S., MOTTO, Michael G., PATEL, Mahendra R., SIMONELLI, Anthony P. and DAVE, Rutesh H. Evaluation of Hydroxypropyl Methylcellulose Matrix Systems as Swellable Gastro-Retentive Drug Delivery Systems (GRDDS)**. Journal of Pharmaceutical Sciences**. v. 100, n. 1, p. 150–163. 2011. DOI 10.1002/jps.22252.

20. BEKAROĞLU, Maide Gökçe, İŞÇI, Yavuz and İŞÇI, Sevim. Colloidal properties and in vitro evaluation of Hydroxy ethyl cellulose coated iron oxide particles for targeted drug delivery**. Materials Science and Engineering: C**. v. 78, p. 847–853. 2017. DOI 10.1016/j.msec.2017.04.030.

21. WANG, Feng, WANG, Yu-Cai, YAN, Li-Feng and WANG, Jun. Biodegradable vesicular nanocarriers based on poly(ε-caprolactone)-block-poly(ethyl ethylene phosphate) for drug delivery**. Polymer**. v. 50, n. 21, p. 5048–5054. 2009. DOI 10.1016/j.polymer.2009.09.007.

22. WANG, Weiwei, DENG, Liandong, LIU, Shasha, LI, Xu, ZHAO, Xiumei, HU, Renjie, ZHANG, Jianhua, HAN, Haijie and DONG, Anjie. Adjustable degradation and drug release of a thermosensitive hydrogel based on a pendant cyclic ether modified poly(ε-caprolactone) and poly(ethylene glycol)co-polymer**. Acta Biomaterialia**. v. 8, n. 11, p. 3963–3973. 2012. DOI 10.1016/j.actbio.2012.07.021.

23. BAINS, Aman, WULFF, Jeremy E. and MOFFITT, Matthew G. Microfluidic synthesis of dye-loaded polycaprolactone-block-poly(ethylene oxide) nanoparticles: Insights into flow-directed loading and in vitro release for drug delivery**. Journal of Colloid and Interface Science**. v. 475, p. 136–148. 2016. DOI 10.1016/j.jcis.2016.04.010.

24. PRABAHARAN, Mani, GRAILER, Jamison J., PILLA, Srikanth, STEEBER, Douglas A. and GONG, Shaoqin. Folate-conjugated amphiphilic hyperbranched block copolymers based on Boltorn® H40, poly(l-lactide) and poly(ethylene glycol) for tumor-targeted drug delivery**. Biomaterials**. v. 30, n. 16, p. 3009–3019. 2009. DOI 10.1016/j.biomaterials.2009.02.011.

25. EFTHIMIADOU, E. K., TZIVELEKA, L.-A., BILALIS, P. and KORDAS, G. Novel PLA modification of organic microcontainers based on ring opening polymerization: Synthesis, characterization, biocompatibility and drug loading/release properties**. International Journal of Pharmaceutics**. v. 428, n. 1, p. 134–142. 2012. DOI 10.1016/j.ijpharm.2012.02.030.

26. YANG, Yan, BAJAJ, Nimisha, XU, Peisheng, OHN, Kimberly, TSIFANSKY, Michael D. and YEO, Yoon. Development of highly porous large PLGA microparticles for pulmonary drug delivery**. Biomaterials**. v. 30, n. 10, p. 1947–1953. 2009. DOI 10.1016/j.biomaterials.2008.12.044.

27. PARVEEN, Suphiya and SAHOO, Sanjeeb K. Long circulating chitosan/PEG blended PLGA nanoparticle for tumor drug delivery**. European Journal of Pharmacology**. v. 670, n. 2, p. 372–383. 2011. DOI 10.1016/j.ejphar.2011.09.023.

28. CRUCHO, Carina I. C. and BARROS, Maria Teresa. Formulation of functionalized PLGA polymeric nanoparticles for targeted drug delivery**. Polymer**. v. 68, p. 41–46. 2015. DOI 10.1016/j.polymer.2015.04.083.

29. SARAVANAKUMAR, Kandasamy, HU, Xiaowen, SHANMUGAM, Sabarathinam, CHELLIAH, Ramachandran, SEKAR, Ponarulselvam, OH, Deog-Hwan, VIJAYAKUMAR, Sekar, KATHIRESAN, Kandasamy and WANG, Myeong-Hyeon. Enhanced cancer therapy with pH-dependent and aptamer functionalized doxorubicin loaded polymeric (poly D, L-lactic-co-glycolic acid) nanoparticles**. Archives of Biochemistry and Biophysics**. v. 671, p. 143–151. 2019. DOI 10.1016/j.abb.2019.07.004.

30. LIMA, Hugo H. C. [de, KUPFER, Vicente L., MOISÉS, Murilo P., GUILHERME, Marcos R., RINALDI, Jaqueline [de C., FELISBINO, Sérgio L., RUBIRA, Adley F. and RINALDI, Andrelson W. Bionanocomposites based on mesoporous silica and alginate for enhanced drug delivery**. Carbohydrate Polymers**. v. 196, p. 126–134. 2018. DOI 10.1016/j.carbpol.2018.04.107.

31. BANSAL, Kuldeep K., GUPTA, Jitendra, ROSLING, Ari and ROSENHOLM, Jessica M. Renewable poly(δ-decalactone) based block copolymer micelles as drug delivery vehicle: in vitro and in vivo evaluation**. Saudi Pharmaceutical Journal**. v. 26, n. 3, p. 358–368. 2018. DOI 10.1016/j.jsps.2018.01.006.

32. JAVANBAKHT, Siamak and NAMAZI, Hassan. Doxorubicin loaded carboxymethyl cellulose/graphene quantum dot nanocomposite hydrogel films as a potential anticancer drug delivery system**. Materials Science and Engineering: C**. v. 87, p. 50–59. 2018. DOI 10.1016/j.msec.2018.02.010.

33. WRONA, Magdalena, CRAN, Marlene J., NERÍN, Cristina and BIGGER, Stephen W. Development and characterisation of HPMC films containing PLA nanoparticles loaded with green tea extract for food packaging applications**. Carbohydrate Polymers**. v. 156, p. 108–117. 2017. DOI 10.1016/j.carbpol.2016.08.094.

34. MÜLLERS, Katrin C., WAHL, Martin A. and PINTO, João F. Production of dosage forms for oral drug delivery by laminar extrusion of wet masses**. European Journal of Pharmaceutics and Biopharmaceutics**. v. 84, n. 3, p. 626–632. 2013. DOI 10.1016/j.ejpb.2013.01.004.

35. MEHUYS, E., VERVAET, C. and REMON, J. P. Hot-melt extruded ethylcellulose cylinders containing a HPMC-Gelucire core for sustained drug delivery**. Journal of Controlled Release: Official Journal of the Controlled Release Society**. v. 94, n. 2–3, p. 273–280. 2004. DOI 10.1016/j.jconrel.2003.09.018.

36. MIRANDA, Janisse Crestani de, MARTINS, Tércio Elyan Azevedo, VEIGA, Francisco and FERRAZ, Humberto Gomes. Cyclodextrins and ternary complexes: technology to improve solubility of poorly soluble drugs**. Brazilian Journal of Pharmaceutical Sciences**. v. 47, n. 4, p. 665–681. 2011. DOI 10.1590/S1984-82502011000400003.

37. CHENG, Liang, GUO, Shengrong and WU, Weiping. Characterization and in vitro release of praziquantel from poly(ε-caprolactone) implants**. International Journal of Pharmaceutics**. v. 377, n. 1, p. 112–119. 2009. DOI 10.1016/j.ijpharm.2009.05.007.

38. FIALHO, Silvia Ligório, BEHAR-COHEN, Francine and SILVA-CUNHA, Armando. Dexamethasone-loaded poly(ε-caprolactone) intravitreal implants: A pilot study**. European Journal of Pharmaceutics and Biopharmaceutics**. v. 68, n. 3, p. 637–646. 2008. DOI 10.1016/j.ejpb.2007.08.004.

39. WEI, XiaWei, GONG, ChangYang, SHI, Shuai, FU, ShaoZhi, MEN, Ke, ZENG, Shi, ZHENG, XiuLing, GOU, MaLing, CHEN, LiJuan, QIU, LiYan and QIAN, ZhiYong. Self-assembled honokiol-loaded micelles based on poly(ε-caprolactone)-poly(ethylene glycol)-poly(ε-caprolactone) copolymer**. International Journal of Pharmaceutics**. v. 369, n. 1, p. 170–175. 2009. DOI 10.1016/j.ijpharm.2008.10.027.

40. ESKITOROS-TOGAY, Ş Melda, BULBUL, Y. Emre, TORT, Serdar, KORKMAZ, Funda [Demirtaş, ACARTÜRK, Füsun and DILSIZ, Nursel. Fabrication of doxycycline-loaded electrospun PCL/PEO membranes for a potential drug delivery system**. International Journal of Pharmaceutics**. v. 565, p. 83–94. 2019. DOI 10.1016/j.ijpharm.2019.04.073.

41. PIAZZA, Rodolfo Debone, BRANDT, João Victor, GOBO, Graciely Gomides, TEDESCO, Antonio Claudio, PRIMO, Fernando Lucas, MARQUES, Rodrigo Fernando Costa and JUNIOR, Miguel Jafelicci. mPEG-co-PCL nanoparticles: The influence of hydrophobic segment on methotrexate drug delivery**. Colloids and Surfaces A: Physicochemical and Engineering Aspects**. v. 555, p. 142–149. 2018. DOI 10.1016/j.colsurfa.2018.06.076.

42. LYONS, John G., BLACKIE, Paul and HIGGINBOTHAM, Clement L. The significance of variation in extrusion speeds and temperatures on a PEO/PCL blend based matrix for oral drug delivery**. International Journal of Pharmaceutics**. v. 351, n. 1, p. 201–208. 2008. DOI 10.1016/j.ijpharm.2007.09.041.

43. GU, Ming-qi, YUAN, Xu-bo, KANG, Chun-sheng, ZHAO, Yun-hui, TIAN, Neng-jiang, PU, Pei-yu and SHENG, Jing. Surface biofunctionalization of PLA nanoparticles through amphiphilic polysaccharide coating and ligand coupling: Evaluation of biofunctionalization and drug releasing behavior**. Carbohydrate Polymers**. v. 67, n. 3, p. 417–426. 2007. DOI 10.1016/j.carbpol.2006.06.019.

44. ESSA, Sherief, RABANEL, Jean Michel and HILDGEN, Patrice. Effect of polyethylene glycol (PEG) chain organization on the physicochemical properties of poly(d, l-lactide) (PLA) based nanoparticles**. European Journal of Pharmaceutics and Biopharmaceutics**. v. 75, n. 2, p. 96–106. 2010. DOI 10.1016/j.ejpb.2010.03.002.

45. HOTHO, Andreas, NÜRNBERGER, Andreas and PAASS, Gerhard. A Brief Survey of Text Mining**. Journal for Computational Linguistics and Language Technology**. P. 19–62. 2005.

46. JO, Taeho. **Text Mining**. Springer International Publishing, [no date]. ISBN 978-3-319-91815-0.

47. KUO-YI, Lin. A TEXT MINING APPROACH TO CAPTURE USER EXPERIENCE FOR NEW PRODUCT DEVELOPMENT**. International Journal of Industrial Engineering**. P. 108–121. 2018.

48. RONEN, Feldman and JAMES, Sanger. **The Text Mining Handbook: Advanced Approaches in Analyzing Unstructured Data**. Cambridge University Press, [no date]. ISBN 0-521-83657-3.

49. DRURY, Brett and ROCHE, Mathieu. A survey of the applications of text mining for agriculture**. Computers and Electronics in Agriculture**. v. 163, p. 104864. 2019. DOI 10.1016/j.compag.2019.104864.

50. PRAYOGA, T. and ABRAHAM, J. Health capability: The representation of IoT in health domain among Jakartans. In : **2016 International Conference on Advanced Computer Science and Information Systems (ICACSIS)**. 2016. p. 103–110.

51. MILLER, A. Text Mining Digital Humanities Projects: Assessing Content Analysis Capabilities of Voyant Tools**. Journal of Web Librarianship**. v. 12, n. 3, p. 169–197. 2018. DOI 10.1080/19322909.2018.1479673.

52. MENGIST, Wondimagegn, SOROMESSA, Teshome and LEGESE, Gudina. Method for conducting systematic literature review and meta-analysis for environmental science research**. MethodsX**. v. 7, p. 100777. 2020. DOI 10.1016/j.mex.2019.100777.

53. SPITALE, Giovanni. Making sense in the flood. How to cope with the massive flow of digital information in medical ethics**. Heliyon**. v. 6, n. 7, p. e04426. 2020. DOI 10.1016/j.heliyon.2020.e04426.

54. MAUREE, Dasaraden, NABONI, Emanuele, COCCOLO, Silvia, PERERA, A.T.D., NIK, Vahid M. and SCARTEZZINI, Jean-Louis. A review of assessment methods for the urban environment and its energy sustainability to guarantee climate adaptation of future cities**. Renewable and Sustainable Energy Reviews**. v. 112, p. 733–746. 2019. DOI 10.1016/j.rser.2019.06.005.

55. EZOJI, Amer and MATTA, Nada. Identification of Territorial Resources Based on Domain Ontology (DOTK) for Sustainability**. 9th IFAC Conference on Manufacturing Modelling, Management and Control MIM 2019**. v. 52, n. 13, p. 683–688. 2019. DOI 10.1016/j.ifacol.2019.11.132.

56. STÉNS, Anna and MÅRALD, Erland. “Forest property rights under attack”: Actors, networks and claims about forest ownership in the Swedish press 2014–2017**. Forest Policy and Economics**. v. 111, p. 102038. 2020. DOI 10.1016/j.forpol.2019.102038.

57. JEONG, Yujin, PARK, Inchae and YOON, Byungun. Identifying emerging Research and Business Development (R&BD) areas based on topic modeling and visualization with intellectual property right data**. Technological Forecasting and Social Change**. v. 146, p. 655–672. 2019. DOI https://doi.org/10.1016/j.techfore.2018.05.010.

58. MA, Jing, ABRAMS, Natalie F., PORTER, Alan L., ZHU, Donghua and FARRELL, Dorothy. Identifying translational indicators and technology opportunities for nanomedical research using tech mining: The case of gold nanostructures**. Technological Forecasting and Social Change**. v. 146, p. 767–775. 2019. DOI https://doi.org/10.1016/j.techfore.2018.08.002.

59. ROBINSON, Douglas K. R., LAGNAU, Axel and BOON, Wouter P. C. Innovation pathways in additive manufacturing: Methods for tracing emerging and branching paths from rapid prototyping to alternative applications**. Technological Forecasting and Social Change**. v. 146, p. 733–750. 2019. DOI https://doi.org/10.1016/j.techfore.2018.07.012.

60. ZHOU, Xiao, HUANG, Lu, PORTER, Alan and VICENTE-GOMILA, Jose M. Tracing the system transformations and innovation pathways of an emerging technology: Solid lipid nanoparticles**. Technological Forecasting and Social Change**. v. 146, p. 785–794. 2019. DOI https://doi.org/10.1016/j.techfore.2018.04.026.

61. PEZZINI, Anderson. MINERAÇÃO DE TEXTOS: CONCEITO, PROCESSO E APLICAÇÕES. In : . 2017.

62. LUCINI, Filipe R., TONETTO, Leandro M., FOGLIATTO, Flavio S. and ANZANELLO, Michel J. Text mining approach to explore dimensions of airline customer satisfaction using online customer reviews**. Journal of Air Transport Management**. v. 83, p. 101760. 2020. DOI https://doi.org/10.1016/j.jairtraman.2019.101760.

63. SUN, Wencheng, CAI, Zhiping, LI, Yangyang, LIU, Fang, FANG, Shengqun and WANG, Guoyan. Data Processing and Text Mining Technologies on Electronic Medical Records: A Review**. TOLLIS, Ioannis G. (ed.), Journal of Healthcare Engineering**. v. 2018, p. 4302425. 2018. DOI 10.1155/2018/4302425.

64. LI, Ji, LOWE, Dan, WAYMENT, Luke and HUANG, Qingrong. Text mining datasets of β-hydroxybutyrate (BHB) supplement products' consumer online reviews**. Data in Brief**. v. 30, p. 105385. 2020. DOI https://doi.org/10.1016/j.dib.2020.105385.

65. VILLENEUVE, Hannah and O'BRIEN, William. Listen to the guests: Text-mining Airbnb reviews to explore indoor environmental quality**. Building and Environment**. v. 169, p. 106555. 2020. DOI 10.1016/j.buildenv.2019.106555.

66. LEE, Jae-hyuck, PARK, Hong-jun, KIM, Ilkwon and KWON, Hyuk-soo. Analysis of cultural ecosystem services using text mining of residents' opinions**. Ecological Indicators**. v. 115, p. 106368. 2020. DOI 10.1016/j.ecolind.2020.106368.

67. YILDIZ, Tayfun. Examining The Concept of Industry 4.0 Studies Using Text Mining and Scientific Mapping Method**. 3rd WORLD CONFERENCE ON TECHNOLOGY, INNOVATION AND ENTREPRENEURSHIP"INDUSTRY 4.0 FOCUSED INNOVATION, TECHNOLOGY, ENTREPRENEURSHIP AND MANUFACTURE" June 21-23, 2019**. v. 158, p. 498–507. 2019. DOI 10.1016/j.procs.2019.09.081.

68. PEJIC-BACH, Mirjana, BERTONCEL, Tine, MEŠKO, Maja and KRSTIĆ, Živko. Text mining of industry 4.0 job advertisements**. International Journal of Information Management**. v. 50, p. 416–431. 2020. DOI 10.1016/j.ijinfomgt.2019.07.014.

69. KARAMI, Amir, GHASEMI, Mehdi, SEN, Souvik, MORAES, Marcos F. and SHAH, Vishal. Exploring diseases and syndromes in neurology case reports from 1955 to 2017 with text mining**. Computers in Biology and Medicine**. v. 109, p. 322–332. 2019. DOI 10.1016/j.compbiomed.2019.04.008.

70. RIBEIRO, João, DUARTE, Júlio, PORTELA, Filipe and SANTOS, Manuel F. Automatically detect diagnostic patterns based on clinical notes through Text Mining**. The 10th International Conference on Emerging Ubiquitous Systems and Pervasive Networks (EUSPN-2019) / The 9th International Conference on Current and Future Trends of Information and Communication Technologies in Healthcare (ICTH-2019) / Affiliated Workshops**. v. 160, p. 684–689. 2019. DOI 10.1016/j.procs.2019.11.027.

71. COOPER, Matthew W., BROWN, Molly E., NILES, Meredith T. and ELQADI, Moataz M. Text mining the food security literature reveals substantial spatial bias and thematic broadening over time**. Global Food Security**. v. 26, p. 100392. 2020. DOI https://doi.org/10.1016/j.gfs.2020.100392.

72. JACINTO, R., REIS, E. and FERRÃO, J. Indicators for the assessment of social resilience in flood-affected communities – A text mining-based methodology**. Science of The Total Environment**. P. 140973. 2020. DOI https://doi.org/10.1016/j.scitotenv.2020.140973.

73. MORO, Alberto, JOANNY, Geraldine and MORETTI, Christian. Emerging technologies in the renewable energy sector: A comparison of expert review with a text mining software**. Futures**. v. 117, p. 102511. 2020. DOI https://doi.org/10.1016/j.futures.2020.102511.

74. HETENYI, Gabor, DR. LENGYEL, Attila and DR. SZILASI, Magdolna. Quantitative analysis of qualitative data: Using voyant tools to investigate the sales-marketing interface**. Journal of Industrial Engineering and Management; Vol 12, No 3 (2019) [online]**. 2019. DOI 10.3926/jiem.2929. Available from: https://www.jiem.org/index.php/jiem/article/view/2929.

75. DICKERSON, Madelynn. **A Gentle Introduction to Text Analysis with Voyant Tools** [online]. [no date]. Accessed 7 August 2020. Available from: https://escholarship.org/content/qt6jz712sf/supp/Dickerson_TextAnalysisVoyantTools_112018.pdf.

76. BAILLIE, Richard T., GEOFFREY BOOTH, G., TSE, Yiuman and ZABOTINA, Tatyana. Price discovery and common factor models**. Price Discovery**. v. 5, n. 3, p. 309–321. 2002. DOI 10.1016/S1386-4181(02)00027-7.

77. BLAND, J Martin and ALTMAN, Douglas G. Statistics Notes: Measurement error and correlation coefficients**. BMJ**. v. 313, n. 7048, p. 41–42. 1996. DOI 10.1136/bmj.313.7048.41.

78. SEDGWICK, Philip. Pearson's correlation coefficient**. BMJ [online]**. v. 345. 2012. DOI 10.1136/bmj.e4483. Available from: https://www.bmj.com/content/345/bmj.e4483.

79. DEMETRESCU, Matei, HASSLER, Uwe and TARCOLEA, Adina-Ioana. Combining Significance of Correlated Statistics with Application to Panel Data***. Oxford Bulletin of Economics and Statistics**. v. 68, n. 5, p. 647–663. 2006. DOI 10.1111/j.1468-0084.2006.00181.x.

80. BEWICK, Viv, CHEEK, Liz and BALL, Jonathan. Statistics review 7: Correlation and regression**. Critical Care**. v. 7, n. 6, p. 451. 2003. DOI 10.1186/cc2401.

81. CURTIN, François and SCHULZ, Pierre. Multiple correlations and bonferroni's correction**. Biological Psychiatry**. v. 44, n. 8, p. 775–777. 1998. DOI 10.1016/S0006-3223(98)00043-2.

82. VASISHTH, Shravan, MERTZEN, Daniela, JÄGER, Lena A. and GELMAN, Andrew. The statistical significance filter leads to overoptimistic expectations of replicability**. Journal of Memory and Language**. v. 103, p. 151–175. 2018. DOI 10.1016/j.jml.2018.07.004.

83. LEEK, Jeffrey T. and PENG, Roger D. Statistics: *P* values are just the tip of the iceberg**. Nature News**. v. 520, n. 7549, p. 612. 2015. DOI 10.1038/520612a.

84. HARI, B. N. [Vedha, REDDY, A. [Brahma and RANI, B. [Samyuktha. Floating Drug Delivery of Nevirapine as a Gastroretentive System**. Journal of Young Pharmacists**. v. 2, n. 4, p. 350–355. 2010. DOI 10.4103/0975-1483.71622.

85. WANG, Chao, CHENG, Liang and LIU, Zhuang. Drug delivery with upconversion nanoparticles for multi-functional targeted cancer cell imaging and therapy**. Biomaterials**. v. 32, n. 4, p. 1110–1120. 2011. DOI 10.1016/j.biomaterials.2010.09.069.

86. LI, Xiaojie, QIAN, Yinfeng, LIU, Tao, HU, Xianglong, ZHANG, Guoying, YOU, Yezi and LIU, Shiyong. Amphiphilic multiarm star block copolymer-based multifunctional unimolecular micelles for cancer targeted drug delivery and MR imaging**. Biomaterials**. v. 32, n. 27, p. 6595–6605. 2011. DOI 10.1016/j.biomaterials.2011.05.049.

87. GULATI, Karan, RAMAKRISHNAN, Saminathan, AW, Moom Sinn, ATKINS, Gerald J., FINDLAY, David M. and LOSIC, Dusan. Biocompatible polymer coating of titania nanotube arrays for improved drug elution and osteoblast adhesion**. Acta Biomaterialia**. v. 8, n. 1, p. 449–456. 2012. DOI 10.1016/j.actbio.2011.09.004.

88. MACHÍN, Rubén, ISASI, José Ramón and VÉLAZ, Itziar. β-Cyclodextrin hydrogels as potential drug delivery systems**. Carbohydrate Polymers**. v. 87, n. 3, p. 2024–2030. 2012. DOI 10.1016/j.carbpol.2011.10.024.

89. GAO, Baojiao, FANG, Li, MEN, Jiying and ZHANG, Yanyan. Preparation of grafted microspheres CPVA-g-PSSS and studies on their drug-carrying and colon-specific drug delivery properties**. Materials Science and Engineering: C**. v. 33, n. 3, p. 1300–1306. 2013. DOI 10.1016/j.msec.2012.12.029.

90. DENG, Haijuan and LEI, Zhongli. Preparation and characterization of hollow Fe3O4/SiO2@PEG–PLA nanoparticles for drug delivery**. Composites Part B: Engineering**. v. 54, p. 194–199. 2013. DOI 10.1016/j.compositesb.2013.05.010.

91. BÉDOUET, Laurent, PASCALE, Florentina, MOINE, Laurence, WASSEF, Michel, GHEGEDIBAN, Saïda H., NGUYEN, Van-Nga, BONNEAU, Michel, LABARRE, Denis and LAURENT, Alexandre. Intra-articular fate of degradable poly(ethyleneglycol)-hydrogel microspheres as carriers for sustained drug delivery**. International Journal of Pharmaceutics**. v. 456, n. 2, p. 536–544. 2013. DOI 10.1016/j.ijpharm.2013.08.016.

92. XU, Xiubin, LÜ, Shaoyu, GAO, Chunmei, WANG, Xinggang, BAI, Xiao, DUAN, Haogang, GAO, Nannan, FENG, Chen and LIU, Mingzhu. Polymeric micelle-coated mesoporous silica nanoparticle for enhanced fluorescent

imaging and pH-responsive drug delivery. **Chemical Engineering Journal**. v. 279, p. 851–860. 2015. DOI 10.1016/j.cej.2015.05.085.

93. HO, Lin-Chen, HSU, Chao-Hsiung, OU, Chung-Mao, WANG, Chia-Wei, LIU, Tsang-Pai, HWANG, Lian-Pin, LIN, Yung-Ya and CHANG, Huan-Tsung. Unibody core–shell smart polymer as a theranostic nanoparticle for drug delivery and MR imaging. **Biomaterials**. v. 37, p. 436–446. 2015. DOI 10.1016/j.biomaterials.2014.10.006.

94. HUANG, Jing, SHU, Qing, WANG, Liya, WU, Hui, WANG, Andrew Y. and MAO, Hui. Layer-by-layer assembled milk protein coated magnetic nanoparticle enabled oral drug delivery with high stability in stomach and enzyme-responsive release in small intestine. **Biomaterials**. v. 39, p. 105–113. 2015. DOI 10.1016/j.biomaterials.2014.10.059.

95. HEMMATI, Khadijeh, SAHRAEI, Razieh and GHAEMY, Mousa. Synthesis and characterization of a novel magnetic molecularly imprinted polymer with incorporated graphene oxide for drug delivery. **Polymer**. v. 101, p. 257–268. 2016. DOI 10.1016/j.polymer.2016.08.074.

96. HEMMATI, Khadijeh, MASOUMI, Arameh and GHAEMY, Mousa. Tragacanth gum-based nanogel as a superparamagnetic molecularly imprinted polymer for quercetin recognition and controlled release. **Carbohydrate Polymers**. v. 136, p. 630–640. 2016. DOI 10.1016/j.carbpol.2015.09.006.

97. HASHEMI-MOGHADDAM, Hamid, KAZEMI-BAGSANGANI, Saeed, JAMILI, Mahdi and ZAVAREH, Saeed. Evaluation of magnetic nanoparticles coated by 5-fluorouracil imprinted polymer for controlled drug delivery in mouse breast cancer model. **International Journal of Pharmaceutics**. v. 497, n. 1, p. 228–238. 2016. DOI 10.1016/j.ijpharm.2015.11.040.

98. BAI, Yang, LIU, Cai-ping, XIE, Fang-yuan, MA, Ran, ZHUO, Long-hai, LI, Na and TIAN, Wei. Construction of β-cyclodextrin-based supramolecular hyperbranched polymers self-assemblies using AB2-type macromonomer and their application in the drug delivery field. **Carbohydrate Polymers**. v. 213, p. 411–418. 2019. DOI 10.1016/j.carbpol.2019.03.017.

99. WANG, Jingyun, XIA, Ying, LIU, Huiying, XIA, Jing, QIAN, Ming, ZHANG, Liuwei, CHEN, Lili and CHEN, Qixian. Poly(lactobionamidoethyl methacrylate)-based amphiphiles with ultrasound-labile components in manufacture of drug delivery nanoparticulates for augmented cytotoxic efficacy to hepatocellular carcinoma. **Journal of Colloid and Interface Science**. v. 551, p. 1–9. 2019. DOI 10.1016/j.jcis.2019.05.008.

100. GAO, Lingyan, ZABIHI, Fatemeh, EHRMANN, Svenja, HEDTRICH, Sarah and HAAG, Rainer. Supramolecular nanogels fabricated via host–guest molecular recognition as penetration enhancer for dermal drug delivery. **Journal of Controlled Release**. v. 300, p. 64–72. 2019. DOI 10.1016/j.jconrel.2019.02.011.