

Antiinflammatory and Wound Healing Activity of Sedum Essential Oils Growing in Kazakhstan

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Abstract—The article represents the results of clinical researches of composite herbal medicinal product based on essential oils of Sedum plants growing in Kazakhstan in commercial reserves at the territory of Kazakhstan. The results of comparative analysis are represented in obstetric-gynecologic practice during combined therapy for postnatal complications, inflammatory infiltrates in the area of surgical wounds including wounds after caesarean section.

Keywords—Anti-inflammatory, bioactive substances, essential oils, isolation, *Sedum L.*, wound healing.

I. INTRODUCTION

IRRESPECTIVE of in-depth study and development of new methods of prevention and treatment of purulent-septic diseases in obstetric-gynecologic practice the decrease in the frequency of this pathology does not take place and as per the data provided by different authors, it amounts up to 65%, they take 2-4 place as the cause of maternal mortality [1].

The last decade the growth of severe and disseminated forms of inflammatory diseases is observed in Kazakhstan, in particular, septic shock, which progresses on 3-15% of patients with infectious complications of postnatal period. In terms of the rate of occurrence septic shock takes third place after hemorrhagic and cardiovascular shock, in terms of lethality it takes first place.

The structure of obstetric sepsis has significantly changed. Currently the first place is taken by postabortive sepsis (40%) that is connected with usage of imperfect methods of artificial termination of pregnancy in late periods (intraamniotic injection of sodium chloride, glucose). The second place is taken by postnatal sepsis (32%); the last place is taken by septic complications of caesarean section (28%).

The nature of microorganisms (their virulence, reproductive rate, bacterial content), the matter of interaction of a microorganism and microflora is important in progress of infectious complications in postoperative period. Moreover, most unfavorable conditions of gestation course, such as anemia, pyelonephritis, tonsillitis, colitis, big blood loss, significantly increase the risk of progress of postoperative infectious diseases as they disturb protective functions of organism [2], [3].

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In this connection, search for and assessment of effectiveness of new medicines for treatment of postoperative infectious complications, having biostimulating effect and speeding up regeneration processes, is very promising and topical.

The purpose of this research was assessment of effectiveness and acceptability of composite herbal medicinal product based on essential oils of Sedum plants growing in Kazakhstan for inflammatory infiltrates in the area of surgical wounds.

Flora of Kazakhstan includes 9 described species of *Sedum L.* plants, 2 species are in commercial reserves: *Sedum ewersii* Ledeb. and *Sedum hybridum L.* *Sedum L.* plants are used since olden times in folk medicine and in homeopathic medicine of different countries. Thus, essential oils of *Sedum acre L.* are used as hypotensive drug, speed up blood coagulation, constrict blood vessels and stimulate heart function. It is used in Tibetan medicine to treat skin cancer, old corns, open wounds. Essential oils of *Sedum aizoon L.* have identical effect. The descriptions of usage of essential oils based on *Sedum L.* in folk medicine in treatment of epilepsy, burns, liver diseases, inflammations of upper respiratory tracts, hemorrhoid, skin cancer, to remove moles, treatment of septic wounds, anemia, treatment of nephritis, fever are available without indication of species [4]. All the above gives evidence of topicality of researches of essential oil fractions of *Sedum L.* species growing in Kazakhstan for introducing them into officinal medicine.

II. MATERIALS AND METHODS

A. Plant Materials

Plant raw materials were collected in the foothill of Zailiyskiy Alatau (the Republic of Kazakhstan) in blossoming period in July 2013. Essential oil was obtained by the method hydrodistillation air-dry aerial part of *Sedum L.* plants using Clevenger apparatus within 3 hours [5].

B. Essential Oils Production

Pilot batch of plant medicinal product based on Sedum essential oils was produced by Chimpharm JSC, Santo Member of Polpharma Group (Kazakhstan). The following tests were conducted for the medicine: radiation control, microbial enumeration test, acute and chronic toxicity has been analyzed.

C. Clinical Testing

Characteristic of the analyzed group: during clinical test of the plant medicinal product based on Sedum essential oils 37

female patients at the age from 35 to 57 with clinical signs of complicated postoperative processes were examined. Complaints on pain in the area of postoperative sutures had all female patients. Oedema of tissues in the area of sutures was on 15 female patients (40.5%), oedema and hyperemia was on 16 female patients (43.3%), partial surgical suture line disruption was on 6 women that amounted to 16.2%. On 2 out of 37 (5.4%) patients, surgical suture line disruption was accompanied by body temperature increase up to 37.7 °C, chilly sensation, and general uneasiness. In medical history of 26 female patients (70.3%) chronic sites of infection – chronic tonsillitis, pyelonephritis, adnexitis was observed. On all patients before and after treatment the blood was analyzed for leukocytosis, ESR, smear bacterioscopic analysis were performed, some components of humoral immune system were determined [6].

Moreover, 12 new mothers with clinical signs of inflammatory process on sutures on anterior abdominal wall after caesarean section and partial disruption of surgical suture line on perineum were examined. General clinical test, bacterioscopic test of wound fluid was performed to all female patients, medical history data was taken into account; wound cleansing time, diminishment of infiltrate, granulation was taken into account [7].

Effectiveness of treatment was analyzed based on disappearance or diminishment of oedema and hyperemia of tissues, records of blood inflammatory response parameters, data on bacterioscopic analysis of wound fluid [6].

Medicine usage methods - surgical wound treatment 2 times a day, treatment with other medicines of local action was not performed.

Before and after treatment general clinical test, determination of immune status, bacterioscopic test of wound fluid was performed to all women, medical history data was taken into account, wound cleansing and healing time, full granulations, side effects and complications, satisfaction with the used medicine was assessed [6].

Effectiveness, safety and tolerance to plant medicinal product tolerance based on Sedum essential oils was analyzed based on disappearance or diminishment of inflammatory infiltrate, oedema, wound hyperemia, analysis of frequency and character of side effects and complications, analysis of parameters of inflammatory response of blood (leukocytosis, white blood cell count, ESR) immune status and data on bacterioscopic test of wound fluid [6]-[8].

Reference medicinal product is Levomekol 5% ointment produced by Nizhpharm (Russia).

D. Statistical Analysis

Statistic processing on the obtained results was performed in accordance with generally accepted methods of medical statistics.

III. RESULTS AND DISCUSSION

On female patients with inflammatory infiltration and partial disruption of surgical suture line anesthetic wound healing effect of plant medicinal product based on Sedum

essential oils was observed as early as on the second day after beginning of using it, wound cleansing took place, as a rule, within the first row days. Hyperemia in the area of suture line also was not observed for 2-3-d day of usage of medicine, good constant course was observed. The absence of clinical effect on this group of patients was not registered.

TABLE I
THE DYNAMICS OF CLINICAL, LABORATORY FINDINGS AND INSTRUMENTATION DATA ON THE PATIENTS - UPON ADMISSION

Indicators	Main group		Control group	
	number	%	number	%
Skin itching				
- no signs	-	-	-	-
- mild signs	6	16.3	7	20.0
- moderate signs	14	37.8	6	17.1
- severe signs	17	45.9	18	51.4
Oedema				
- no signs	-	-	-	-
- mild signs	3	8.1	4	11.4
- moderate signs	19	51.4	24	68.5
- severe signs	15	40.5	17	48.5
Hyperemia				
- no signs	-	-	-	-
- mild signs	9	24.3	10	28.5
- moderate signs	12	32.4	14	40.0
- severe signs	16	43.3	16	45.7
Leukocytosis				
- no signs (0)	-	-	-	-
- mild signs (1)	10	27.0	8	22.8
- moderate signs (2)	8	21.6	13	37.1
- severe signs (3)	19	51.4	14	40.0
White blood cell count				
- no signs	-	-	-	-
- mild signs	9	24.3	11	31.4
- moderate signs	10	27.0	9	25.7
- severe signs	18	48.7	15	42.8
ESR				
- no signs	-	-	-	-
- mild signs	9	24.3	7	20.0
- moderate signs	10	27.0	9	25.7
- severe signs	18	48.6	19	54.3
Bacterioscopy of wound content				
- no signs	-	-	-	-
- mild signs	4	10.8	1	2.8
- moderate signs	15	40.5	14	40.0
- severe signs	18	48.7	20	57.1

New mothers at the age from 19 to 40 with clinical signs of complicated wound process after caesarean section and perineum: 5 – after caesarean section, 7 – with complicated wound process on perineum. All female patients had complaints on pain in the area of suture lines. Clinical signs of suture inflammation on perineum were on all female patients in 100% of cases. Partial disruption of the suture lines on perineum on 3 (42.8%) female patients. On female patients after caesarean section in disruption of suture line was in 2 cases (40%), in 2 cases suture lines were separated (40%). In 100% of cases, that is all new mothers had clinical signs of inflammation after caesarean section. Mild or moderate anemia in medical history of 9 (75%) of female patients, kidney diseases were in medical history of 5 (41.6%) female patients. Gestation course was complicated with gestational toxicosis on 58.3%, coleitis on 33.3%, sexually transmitted diseases – on 25%. On 4 (80%) female patients caesarean section was performed in an expedited manner, on 2(28.6%)

female patients had disruption of perineum of first and second degree; episiotomy was performed on 5 (71.4%) female patients.

TABLE II
THE DYNAMICS OF CLINICAL, LABORATORY FINDINGS AND INSTRUMENTATION DATA ON THE PATIENTS - ON FIFTH DAY

Indicators	Main group		Control group	
	number	%	number	%
Skin itching				
- no signs	-	-	-	-
- mild signs	27	72.9	22	62.8
- moderate signs	7	18.9	7	20.0
- severe signs	3	8.2	6	17.1
Oedema				
- no signs	-	-	-	-
- mild signs	26	70.2	18	51.4
- moderate signs	9	24.3	11	31.4
- severe signs	2	5.4	6	17.1
Hyperemia				
- no signs	-	-	-	-
- mild signs	27	72.9	16	45.7
- moderate signs	8	21.6	12	34.3
- severe signs	2	5.4	8	22.8
Leukocytosis				
- no signs (0)	-	-	-	-
- mild signs (1)	21	56.7	14	40.0
- moderate signs (2)	10	27.0	11	31.4
- severe signs (3)	6	16.3	10	28.5
White blood cell count				
- no signs	-	-	-	-
- mild signs	20	54.0	18	51.4
- moderate signs	11	29.7	8	22.8
- severe signs	6	16.3	9	25.7
ESR				
- no signs	-	-	-	-
- mild signs	25	67.6	19	54.3
- moderate signs	8	21.6	10	28.5
- severe signs	4	10.8	6	17.1
Bacterioscopy of wound content				
- no signs	-	-	-	-
- mild signs	27	72.9	23	65.7
- moderate signs	7	18.8	8	22.8
- severe signs	3	8.2	4	11.4
Satisfaction with used medicine				
- no signs	-	-	-	-
- mild signs	0	0	1	2.8
- moderate signs	11	29.7	9	25.7
- severe signs	26	70.3	25	71.4
Nature of side effects				
	no		no	

In complete blood count decrease in leukocytosis from 12.5 $0.3 \cdot 10^9 / l$ to 9.7 $0.2 \cdot 10^9 / l$ and normalization of parameters of white blood cell count was observed on 3-d days starting from the beginning of treatment. Bacterioscopic analysis of wound fluid before treatment gave evidence of bacterial contamination with pathogenic microflora (streptococci, staphylococci etc.) in 33.3%, oedema and cell hypertrophy as well as increase in the content of leukocytes was observed on all female patients. After treatment it was observed that the number of modified cells adequately decreased, there was no inflammatory response of epithelium.

During the analysis of initial immunogram on the majority of female patients (77.7%) the decrease of absolute and relative content of lymphocytes down to 16.6 ± 1.2 was found, in 55.5% of observations increase in serum IgM (24.8 ± 6.7 mg) level was observed. Indicators of immunogram after

treatment: adequate increase in the ratio of lymphocytes ($p < 0.05$), increase in the content of lymphocytes up to the lower normal values as well as normalization of serum IgM level [see in Tables I-III].

The represented data give evidence of that clinical effect was accompanied with normalization of changed laboratory findings.

No allergic responses or side effects were observed during usage of the plant medicinal products based on *Sedum L.* essential oils.

TABLE III
THE DYNAMICS OF CLINICAL, LABORATORY FINDINGS AND INSTRUMENTATION DATA ON THE PATIENTS - IN 2 WEEKS

Indicators	Main group		Control group	
	number	%	number	%
Skin itching				
- no signs	-	-	-	-
- mild signs	35	94.6	30	85.7
- moderate signs	2	5.4	4	11.4
- severe signs	0	0	1	2.8
Oedema				
- no signs	-	-	-	-
- mild signs	37	100	29	82.8
- moderate signs	0	0	5	14.2
- severe signs	0	0	1	2.8
Hyperemia				
- no signs	-	-	-	-
- mild signs	37	100	31	88.5
- moderate signs	0	0	3	8.5
- severe signs	0	0	1	2.8
Leukocytosis				
- no signs (0)	-	-	-	-
- mild signs (1)	37	100	29	82.8
- moderate signs (2)	0	0	5	14.2
- severe signs (3)	0	0	1	2.8
White blood cell count				
- no signs	-	-	-	-
- mild signs	37	100	29	82.8
- moderate signs	0	0	5	14.2
- severe signs	0	0	1	2.8
ESR				
- no signs	-	-	-	-
- mild signs	36	97.3	31	88.5
- moderate signs	1	2.7	3	8.5
- severe signs	0	0	1	2.8
Bacterioscopy of wound content				
- no signs	-	-	-	-
- mild signs	37	100	33	94.2
- moderate signs	0	0	2	5.7
- severe signs	0	0	1	2.8
Satisfaction with used medicine				
- no signs	-	-	-	-
- mild signs	0	0	0	0
- moderate signs	0	0	5	14.2
- severe signs	37	100	30	85.7
Nature of side effects				
	no		no	

In addition, during clinical tests comparative analysis of the efficiency of plant medicinal product based on *Sedum* essential oils and Levomekol ointment was performed. For that, two groups of female patients were examined with clinical signs of inflammatory process in the area of surgical wounds: main group ($n=37$) treated with the plant medicinal product developed by us and control group ($n=35$) treated with Levomekol ointment. Comparative assessment of these medicines was performed based on disappearance or

diminishment of inflammatory infiltrate, oedema, wound hyperemia, analysis of frequency and character of side effects and complications, analysis of parameters of blood inflammatory response (leukocytosis, white blood cell count, ESR) and data on bacterioscopic analysis of wound fluid [see in Table IV]:

TABLE IV
COMPARISON OF EFFECTIVENESS OF PLANT MEDICINAL PRODUCT BASED ON
SEDUM L. ESSENTIAL OILS AND LEVOMEKOL MEDICINE

Effects of action	Period of effect	
	<i>Sedum L.</i> essential oils (n=37)	Levomekol (n=35)
Surgical wound cleansing	2 th day	3 th day
Surgical wound oedema	2 th day	3 th day
Hyperemia in the area of surgical sutures	3 th day	4 th day
Decrease in leukocytosis	3 th day	4 th day
Normalization of Ig M level	3 th day	4 th day

On female patients with inflammatory infiltration and partial surgical suture line disruption, wound healing effect of *Sedum* essential oils was observed on the second day after beginning of usage of plant medicinal product; wound was cleansed as a rule, during the first 2 days. Hyperemia in the area of suture was also not observed on 2-3 days of usage of this medicine with good constant dynamics. Identical effects were observed during usage of Levomekol ointment, but not earlier than on 3-4 day after usage of it.

In complete blood count decrease in leukocytosis and normalization of white blood cell count during usage of plant medicinal product based on *Sedum* essential oil was observed on third day starting from the beginning of treatment. Whereas during usage of Levomekol ointment; similar effect was observed not earlier than on fourth day of treatment. Bacterioscopy of wound fluid before treatment gave evidence of bacterial contamination with pathogenic microflora. On all patients, increase in the content of leukocytes in wound fluid, oedema and cell hypertrophy was observed. After treatment with both medicines it was observed that the number of modified cells definitely decreased, there was no inflammatory reaction of epithelium.

IV. CONCLUSION

Clinical effectiveness of plant medicinal product based on *Sedum L.* essential oils in treatment of purulent-septic disease in obstetric-gynecological practice is higher compared to Levomekol ointment.

Plant medicinal product based on *Sedum L.* essential oils has high anti-inflammatory effect, it is a means for external treatment of inflammatory processes in postoperative period, and it is convenient in usage, well tolerated by patients, does not cause side effects and can be recommended for widespread use in practice.

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REFERENCES

- [1] G. R. G. Monfis, D. A. Baker, *Infectious diseases in obstetrics and gynecology*, London: CRC Press, 2004.
- [2] S. Faro, *Clin. Obstet. Gynecol.*, vol. 55, no. 4, pp. 875-887, 2012.
- [3] F. Paruk, C. Care, *Best Pract. Res. Clin. Obstet. Gynecol.*, vol. 22, no. 5, pp. 865-883, 2008.
- [4] D. A. Muraveva, *Pharmacognosy*, Moscow: Medicine, 2007.
- [5] R. A. Muzychkina, D. Yu. Korulkin, *Bioactive constituents of plants. Extraction, separation and analysis*, Almaty: Atamura, 2006.
- [6] H. G. Vogel, J. Maas, A. Gebauer, *Drug Discovery and Evaluation: Methods in Clinical Pharmacology*, Berlin: Springer, 2011.
- [7] S. K. Gupta, *Drug Screening Methods*, Kent: Anshan Publishers, 2009.
- [8] J. Kolman, P. Meng, G. Scott, *Good clinical practice: standard operating procedures for clinical researchers*, New-York: J. Wiley & Sons, 1998.